| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 148.15 | 148.36 |

FILE 'CAPLUS' ENTERED AT 11:10:20 ON 04 JUN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 4 Jun 2003 VOL 138 ISS 23
FILE LAST UPDATED: 3 Jun 2003 (20030603/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:946287 CAPLUS
DOCUMENT NUMBER: 138:13982
TITLE: Preparation of 2-trifluoromethylpurines as phosphodiesterase IV inhibitors
INVENTOR(S): Liu, Ruiping; Hess, Hans-Juergen Ernst; Hopper, Allen; Rong, Yajing; Tehim, Ashok
PATENT ASSIGNEE(S): Memory Pharmaceuticals Corporation, USA
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| WO 2002098878 | A1 | 20021212 | WO 2002-US22509 | 20020208 |
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| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2003045533 | A1 | 20030306 | US 2002-67996 | 20020208 |

PRIORITY APPLN. INFO.: US 2001-267195P P 20010208
US 2002-344824P P 20020107
OTHER SOURCE(S): MARPAT 138:13982
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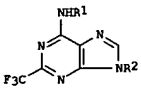
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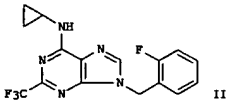
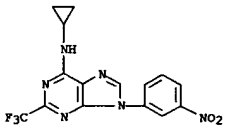

II

AB 2-Trifluoromethylpurines, such as I [R1 = H, alkyl, cycloalkyl, etc.; R2 = alkyl, cycloalkyl, aryl, arylalkyl, heteroaryl, etc.], were prepd. for therapeutic use as phosphodiesterase IV (PDE4) inhibitors for the treatment of disorders, such as memory impairment due to Alzheimer's disease, schizophrenia, Parkinson's disease, Huntington's disease, Pick's disease, Creutzfeldt-Jakob disease, depression, aging, head trauma, stroke, CNS hypoxia, cerebral senility, multi-infarct dementia, HIV or cardiovascular disease. Thus, purine II was prepd. via a series of synthetic steps which included cyclocondensation of F3CCN with 5-aminoimidazole-4-carboxamide hydrochloride by refluxing at 160-165.degree. for 4 h to form 2-(trifluoromethyl)hypoxanthine, chlorination of the hypoxanthine using SOCl2 in CHCl3 to form 6-chloro-2-trifluoromethylpurine, N9-benzylation of the chloropurine with F-2-C6H4CH2Br using K2CO3 in DMF, and finally, amination of the N9-benzylated chloropurine with cyclopropanamine by stirring in EtOH for 16 h. The prepd. purines were assayed for human PDE4 inhibitory activity. Pharmaceutical formulations and dosages of the purines were also discussed.

IT **477725-57-8P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of 2-trifluoromethylpurines as phosphodiesterase IV inhibitors)

RN 477725-57-8 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-(3-nitrophenyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2-trifluoromethylpurines as phosphodiesterase IV inhibitors)

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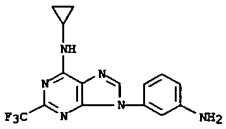

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS (Continued)
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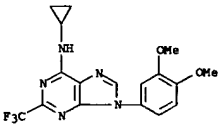

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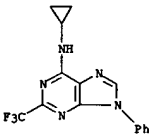

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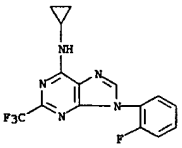
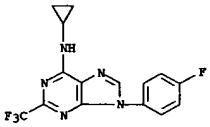


RN 477725-80-7 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-(4-fluorophenyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS (Continued)



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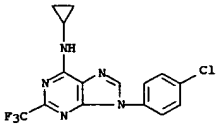

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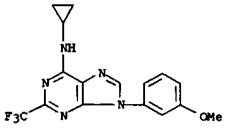

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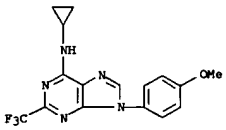

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS (Continued)

RN 477725-88-5 CAPLUS
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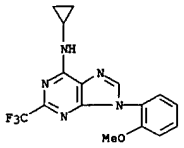

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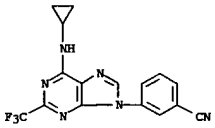

RN 477725-90-9 CAPLUS
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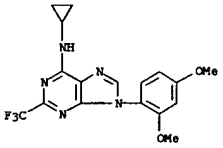
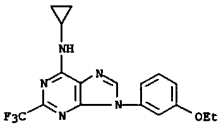


RN 477725-95-4 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-[4-(dimethylamino)phenyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS (Continued)



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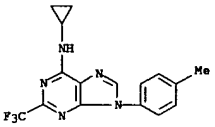
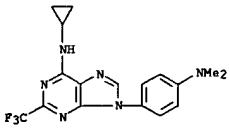


REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS (Continued)



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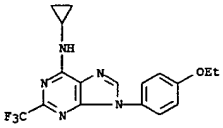

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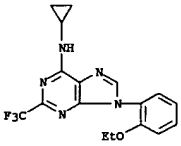

RN 477726-06-0 CAPLUS
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| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
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| FULL ESTIMATED COST | 4.95 | 153.31 |

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| CA SUBSCRIBER PRICE | -0.65 | -0.65 |

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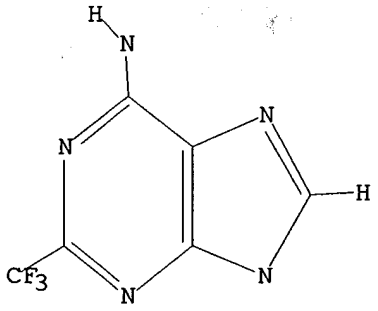

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FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
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PROJECTED ANSWERS: 7 TO 298

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L3 113 SEA SSS FUL L1

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COST IN U.S. DOLLARS SINCE FILE ENTRY 148.15 TOTAL SESSION 148.36

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 10:28:08 ON 04 JUN 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 4 Jun 2003 VOL 138 ISS 23
FILE LAST UPDATED: 3 Jun 2003 (20030603/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L4 47 L3

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L4 ANSWER 1 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:946287 CAPLUS
DOCUMENT NUMBER: 138:13982
TITLE: Preparation of 2-trifluoromethylpurines as phosphodiesterase IV inhibitors
INVENTOR(S): Liu, Ruiping; Hess, Hans-Juergen Ernst; Hopper, Allen; Rong, Yajing; Tehim, Ashok
PATENT ASSIGNEE(S): Memory Pharmaceuticals Corporation, USA
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2002098878 | A1 | 20021212 | WO 2002-US22509 | 20020208 |
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| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2003045533 | A1 | 20030306 | US 2002-67996 | 20020208 |
| PRIORITY APPLN. INFO.: | | | US 2001-267195P P | 20010208 |
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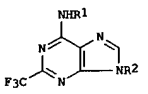
OTHER SOURCE(S): MARPAT 138:13982
GI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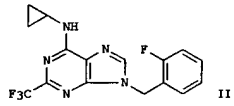
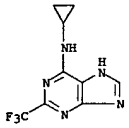

II

AB 2-Trifluoromethylpurines, such as I [R1 = H, alkyl, cycloalkyl, etc.; R2 = alkyl, cycloalkyl, aryl, arylalkyl, heteroaryl, etc.], were prepd. for therapeutic use as phosphodiesterase IV (PDE4) inhibitors for the treatment of disorders, such as memory impairment due to Alzheimer's disease, schizophrenia, Parkinson's disease, Huntington's disease, Pick's disease, Creutzfeldt-Jakob disease, depression, aging, head trauma, stroke, CNS hypoxia, cerebral senility, multi-infarct dementia, HIV or cardiovascular disease. Thus, purine II was prepd. via a series of synthetic steps which included cyclocondensation of F3CCN with 5-aminoimidazole-4-carboxamide hydrochloride by refluxing at 160-165.degree. for 4 h to form 2-(trifluoromethyl)hypoxanthine, chlorination of the hypoxanthine using SOCl2 in CHCl3 to form 6-chloro-2-trifluoromethylpurine, N9-benzylation of the chloropurine with F-2-C6H4CH2Br using K2CO3 in DMF, and finally, amination of the N9-benzylated chloropurine with cyclopropanamine by stirring in EtOH for 16 h. The prepd. purines were assayed for human PDE4 inhibitory activity. Pharmaceutical formulations and dosages of the purines were also discussed.

IT **195252-70-1P 477725-54-5P 477725-57-8P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of 2-trifluoromethylpurines as phosphodiesterase IV inhibitors)

RN 195252-70-1 CAPLUS
CN 1H-Purin-6-amine, N-cyclopropyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



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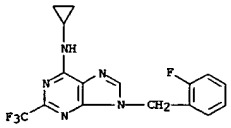

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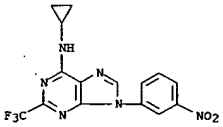

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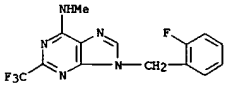
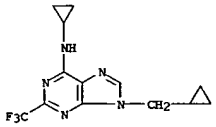
**477725-91-0P 477725-92-1P 477725-93-2P**
**477725-94-3P 477725-95-4P 477725-96-5P**
**477725-97-6P 477725-98-7P 477725-99-8P**
**477726-00-4P 477726-01-5P 477726-02-6P**
**477726-03-7P 477726-04-8P 477726-05-9P**
**477726-06-0P 477726-07-1P 477726-08-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 2-trifluoromethylpurines as phosphodiesterase IV inhibitors)

RN 190377-71-0 CAPLUS
CN 9H-Purin-6-amine, 9-[(2-fluorophenyl)methyl]-N-methyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 195252-47-2 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-(cyclopropylmethyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

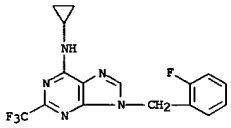




RN 477725-55-6 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-[(2-fluorophenyl)methyl]-2-(trifluoromethyl)-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 477725-54-5
CMF C16 H13 F4 N5

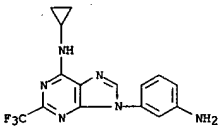


CM 2

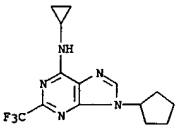
CRN 75-75-2
CMF C H4 O3 S

RN 477725-56-7 CAPLUS
CN 9H-Purin-6-amine, 9-(3-aminophenyl)-N-cyclopropyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

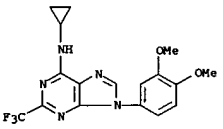
L4 ANSWER 1 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



RN 477725-58-9 CAPLUS
CN 9H-Purin-6-amine, 9-cyclopentyl-N-cyclopropyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

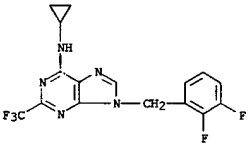


RN 477725-59-0 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-(3,4-dimethoxyphenyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

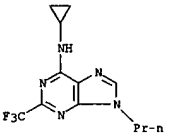


RN 477725-60-3 CAPLUS
CN 9H-Purin-6-amine, N-ethyl-9-[(2-fluorophenyl)methyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

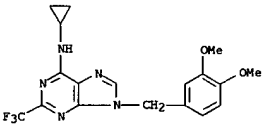
L4 ANSWER 1 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



RN 477725-64-7 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-propyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

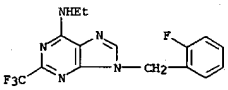


RN 477725-65-8 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-[(3,4-dimethoxyphenyl)methyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

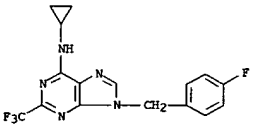


RN 477725-66-9 CAPLUS
CN 9H-Purin-6-amine, 9-(1,3-benzodioxol-5-ylmethyl)-N-cyclopropyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

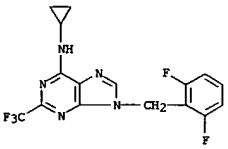
L4 ANSWER 1 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



RN 477725-61-4 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-[(4-fluorophenyl)methyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

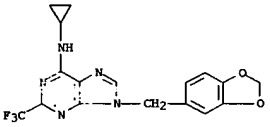


RN 477725-62-5 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-[(2,6-difluorophenyl)methyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

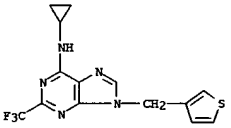


RN 477725-63-6 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-[(2,3-difluorophenyl)methyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

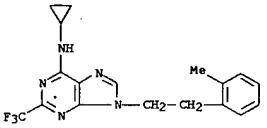
L4 ANSWER 1 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



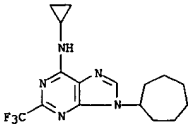
RN 477725-67-0 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-(3-thienylmethyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 477725-68-1 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-[2-(2-methylphenyl)ethyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

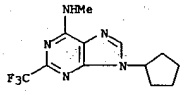


RN 477725-69-2 CAPLUS
CN 9H-Purin-6-amine, 9-cycloheptyl-N-cyclopropyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

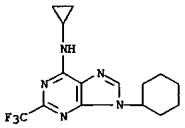


L4 ANSWER 1 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)

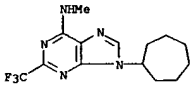
RN 477725-70-5 CAPLUS
CN 9H-Purin-6-amine, 9-cyclopentyl-N-methyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 477725-71-6 CAPLUS
CN 9H-Purin-6-amine, 9-cyclohexyl-N-cyclopropyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

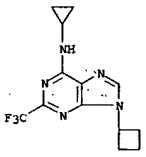


RN 477725-73-8 CAPLUS
CN 9H-Purin-6-amine, 9-cycloheptyl-N-methyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

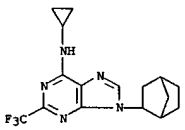


RN 477725-74-9 CAPLUS
CN 9H-Purin-6-amine, 9-(cyclopentylmethyl)-N-cyclopropyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

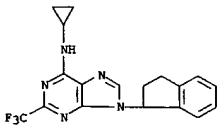
L4 ANSWER 1 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



RN 477725-78-3 CAPLUS
CN 9H-Purin-6-amine, 9-bicyclo[2.2.1]hept-2-yl-N-cyclopropyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

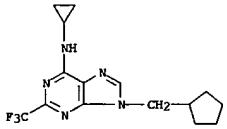


RN 477725-79-4 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-(2,3-dihydro-1H-inden-1-yl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

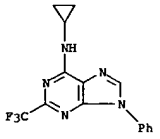


RN 477725-80-7 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-(4-fluorophenyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

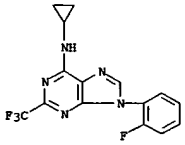
L4 ANSWER 1 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



RN 477725-75-0 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-phenyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

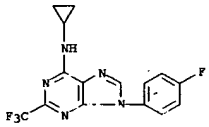


RN 477725-76-1 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-(2-fluorophenyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

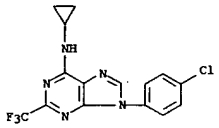


RN 477725-77-2 CAPLUS
CN 9H-Purin-6-amine, 9-cyclobutyl-N-cyclopropyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

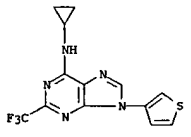
L4 ANSWER 1 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



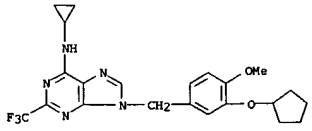
RN 477725-81-8 CAPLUS
CN 9H-Purin-6-amine, 9-(4-chlorophenyl)-N-cyclopropyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 477725-82-9 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-(3-thienyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

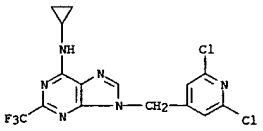


RN 477725-83-0 CAPLUS
CN 9H-Purin-6-amine, 9-[[3-(cyclopentyloxy)-4-methoxyphenyl]methyl]-N-cyclopropyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

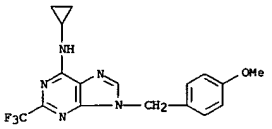


L4 ANSWER 1 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)

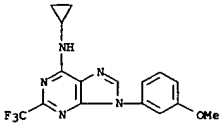
RN 477725-84-1 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-[(2,6-dichloro-4-pyridinyl)methyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 477725-85-2 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-[(4-methoxyphenyl)methyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

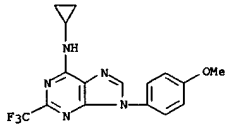


RN 477725-86-3 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-(3-methoxyphenyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

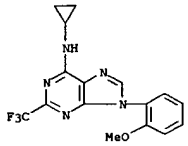


RN 477725-87-4 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-(4-methoxyphenyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

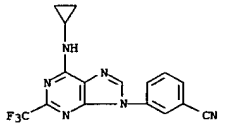
L4 ANSWER 1 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



RN 477725-88-5 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-(2-methoxyphenyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

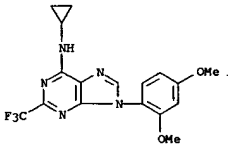


RN 477725-89-6 CAPLUS
CN Benzonitrile, 3-[6-(cyclopropylamino)-2-(trifluoromethyl)-9H-purin-9-yl]- (9CI) (CA INDEX NAME)

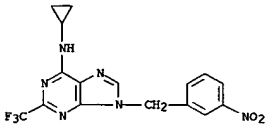


RN 477725-90-9 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-(2,4-dimethoxyphenyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

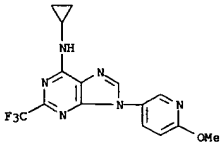
L4 ANSWER 1 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



RN 477725-91-0 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-[(3-nitrophenyl)methyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

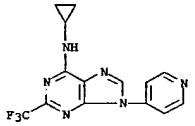


RN 477725-92-1 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-(6-methoxy-3-pyridinyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

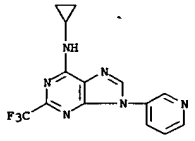


RN 477725-93-2 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-(4-pyridinyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

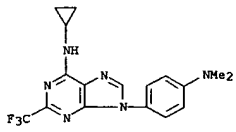
L4 ANSWER 1 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



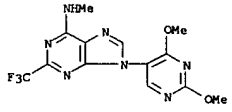
RN 477725-94-3 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-(3-pyridinyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



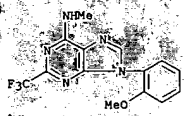
RN 477725-95-4 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-[4-(dimethylamino)phenyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



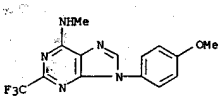
RN 477725-96-5 CAPLUS
CN 9H-Purin-6-amine, 9-(2,4-dimethoxy-5-pyrimidinyl)-N-methyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



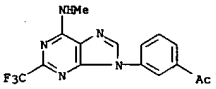
L4 ANSWER 1 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)
RN 477725-97-6 CAPLUS
CN 9H-Purin-6-amine, 9-(2-methoxyphenyl)-N-methyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



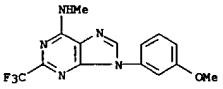
RN 477725-98-7 CAPLUS
CN 9H-Purin-6-amine, 9-(4-methoxyphenyl)-N-methyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 477725-99-8 CAPLUS
CN Ethanone, 1-[3-(6-(methylamino)-2-(trifluoromethyl)-9H-purin-9-yl]phenyl]- (9CI) (CA INDEX NAME)

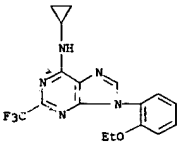


RN 477726-00-4 CAPLUS
CN 9H-Purin-6-amine, 9-(3-methoxyphenyl)-N-methyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

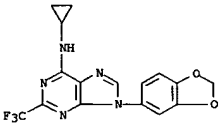


RN 477726-01-5 CAPLUS
CN 9H-Purin-6-amine, N-methyl-9-(3-nitrophenyl)-2-(trifluoromethyl)- (9CI)

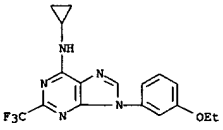
L4 ANSWER 1 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



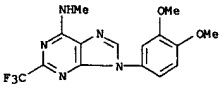
RN 477726-05-9 CAPLUS
CN 9H-Purin-6-amine, 9-(1,3-benzodioxol-5-yl)-N-cyclopropyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 477726-06-0 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-(3-ethoxyphenyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

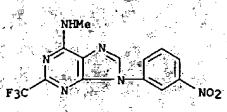


RN 477726-07-1 CAPLUS
CN 9H-Purin-6-amine, 9-(3,4-dimethoxyphenyl)-N-methyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

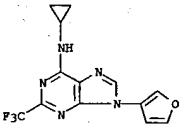


RN 477726-08-2 CAPLUS

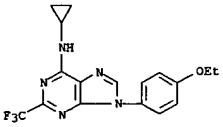
L4 ANSWER 1 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)
(CA INDEX NAME)



RN 477726-02-6 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-(3-furanyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

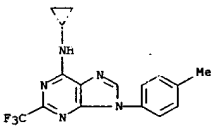


RN 477726-03-7 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-(4-ethoxyphenyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 477726-04-8 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-(2-ethoxyphenyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)
CN 9H-Purin-6-amine, N-cyclopropyl-9-(4-methylphenyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

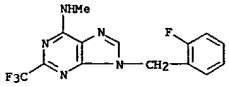


REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:575737 CAPLUS
DOCUMENT NUMBER: 137:135500
TITLE: Methods of inducing ovulation by administering a non-polypeptide cAMP level modulator
INVENTOR(S): Palmer, Stephen; McKenna, Sean; Tepper, Mark; Eshkol, Aliza; MacNamee, Michael C.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 26 pp., Cont.-in-part of U.S. Ser. No. 928,268.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2002103106 | A1 | 20020801 | US 2001-14812 | 20011214 |
| US 2002065324 | A1 | 20020530 | US 2001-928268 | 20010810 |
| PRIORITY APPLN. INFO.: | | | US 2000-224962P P | 20000811 |
| | | | US 2001-928268 A2 | 20010810 |

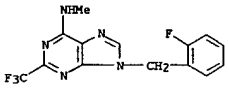
AB The present invention relates to methods of inducing ovulation in a female host comprising the administration of a non-polypeptide cAMP level modulator to the female host. In another aspect, the invention provides for specific administration of the phosphodiesterase inhibitor prior to the luteal phase of the host's ovulatory cycle. Preferred non-polypeptide cAMP level modulator include phosphodiesterase inhibitors, particularly inhibitors of phosphodiesterase 4 isoforms. Pharmaceutical compns. contg. the cAMP modulators are also claimed.
IT **190377-71-0**, NCS 613
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NCS 613; methods of inducing ovulation by administering a non-polypeptide cAMP level modulator)
RN 190377-71-0 CAPLUS
CN 9H-Purin-6-amine, 9-[(2-fluorophenyl)methyl]-N-methyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 3 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:850920 CAPLUS
DOCUMENT NUMBER: 135:367706
TITLE: Method for enhancing cognitive function with phosphodiesterase-4 inhibitors
INVENTOR(S): Hagan, James
PATENT ASSIGNEE(S): Smithkline Beecham P.L.C., UK
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

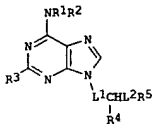
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2001087281 | A2 | 20011122 | WO 2001-GB2134 | 20010515 |
| WO 2001087281 | A3 | 20020328 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| EP 1292287 | A2 | 20030319 | EP 2001-929824 | 20010515 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| PRIORITY APPLN. INFO.: | | | GB 2000-11802 A | 20000516 |
| | | | WO 2001-GB2134 W | 20010515 |

AB A method for enhancing cognitive function by administering to a patient in need thereof an effective amt. of a PDE4 inhibitor.
IT **190377-71-0**, NCS 613
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(enhancing cognitive function with phosphodiesterase-4 inhibitors)
RN 190377-71-0 CAPLUS
CN 9H-Purin-6-amine, 9-[(2-fluorophenyl)methyl]-N-methyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



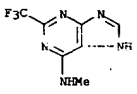
L4 ANSWER 4 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:151488 CAPLUS
DOCUMENT NUMBER: 132:189674
TITLE: Purine derivatives and therapeutic agents containing them for liver diseases
INVENTOR(S): Sakuma, Norisato; Endo, Takeshi; Kobayashi, Tadashi
PATENT ASSIGNEE(S): Zeria Pharmaceutical Co., Ltd., Japan; Nippon Chemiphar Co., Ltd.
SOURCE: Jpn. Kokai Tokkyo Koho, 20 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 2000072773 | A2 | 20000307 | JP 1998-259261 | 19980828 |
| PRIORITY APPLN. INFO.: | | | JP 1998-259261 | 19980828 |
| OTHER SOURCE(S): | | MARPAT 132:189674 | | |
| GI | | | | |

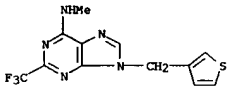


AB The therapeutic agents for hepatitis C, alc. hepatitis, cirrhosis, etc., contain the title derivs. I [R1, R2 = H, (CH2)nR6; R6 = H, C1-6 alkyl, C1-6 alkoxy, C6-12 aryl or 1-4 N, O, and/or S-contg. heteroaryl which may be substituted with 1-5 C1-6 alkyl, C1-6 alkoxy, C6-10 aryl; n = 1-6; R3 = H, halo, CF3, NO2; R4 = H, C1-6 alkyl; R5 = C6-12 aryl or 1-4 N, O, and/or S-contg. heteroaryl which may be substituted with 1-5 C1-6 alkyl, C1-6 alkoxy, halo, NO2, CO2H, OH, amino, C1-6 alkylamino, C6-10 aryl; L1, L2 = direct bond, C1-6 alkylene; if R1 = H, R2 = Me, L1 = L2 = direct bond, and R3 = CF3, then R5 = C6-12 aryl in which benzene ring is substituted with C1-6 alkyl, C1-6 alkoxy, Cl, CO2H, OH, amino, C1-6 alkylamino, C6-10 aryl] and their pharmacol. acceptable salts as active ingredients. 2-Fluoro-6-(methylamino)-9-(3-nitrobenzyl)purine (prepn. given) showed 91.4% inhibition against increase in plasma GPT concn. of mice with Con A-induced hepatic injury.
IT **18925-07-0P 260250-28-0P 260250-29-1P 260250-31-5P 260250-32-6P 260250-37-1P 260250-38-2P 260250-44-0P 260250-46-2P 260250-48-4P 260250-54-2P 260250-55-3P 260250-57-5P 260250-58-6P 260250-59-7P 260250-61-1P 260250-62-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of purine derivs. for treatment of liver diseases)
RN 18925-07-0 CAPLUS

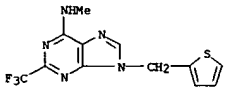
L4 ANSWER 4 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)
CN 1H-Purin-6-amine, N-methyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



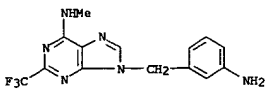
RN 260250-28-0 CAPLUS
CN 9H-Purin-6-amine, N-methyl-9-(3-thienylmethyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 260250-29-1 CAPLUS
CN 9H-Purin-6-amine, N-methyl-9-(2-thienylmethyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

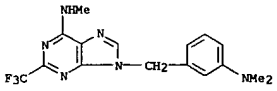


RN 260250-31-5 CAPLUS
CN 9H-Purin-6-amine, 9-[(3-aminophenyl)methyl]-N-methyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

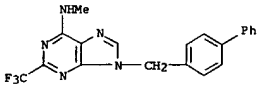


RN 260250-32-6 CAPLUS
CN 9H-Purin-6-amine, 9-[[3-(dimethylamino)phenyl]methyl]-N-methyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

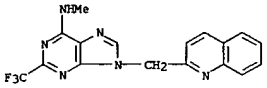
L4 ANSWER 4 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



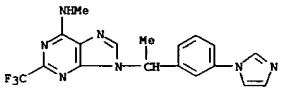
RN 260250-37-1 CAPLUS
CN 9H-Purin-6-amine, 9-([1,1'-biphenyl]-4-ylmethyl)-N-methyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 260250-38-2 CAPLUS
CN 9H-Purin-6-amine, N-methyl-9-(2-quinolinylmethyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

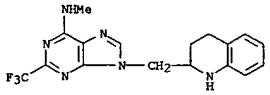


RN 260250-44-0 CAPLUS
CN 9H-Purin-6-amine, 9-[1-[3-(1H-imidazol-1-yl)phenyl]ethyl]-N-methyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

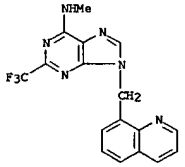


RN 260250-46-2 CAPLUS
CN 9H-Purin-6-amine, N-methyl-9-[(1,2,3,4-tetrahydro-2-quinolinyl)methyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

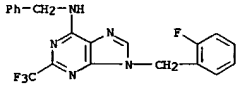
L4 ANSWER 4 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



RN 260250-48-4 CAPLUS
CN 9H-Purin-6-amine, N-methyl-9-(8-quinolinylmethyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

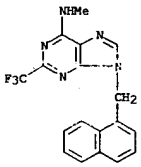


RN 260250-54-2 CAPLUS
CN 9H-Purin-6-amine, 9-[(2-fluorophenyl)methyl]-N-(phenylmethyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

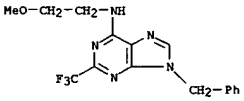


RN 260250-55-3 CAPLUS
CN 9H-Purin-6-amine, N-methyl-9-(1-naphthalenylmethyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

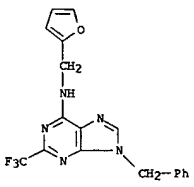
L4 ANSWER 4 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



RN 260250-57-5 CAPLUS
CN 9H-Purin-6-amine, N-(2-methoxyethyl)-9-(phenylmethyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

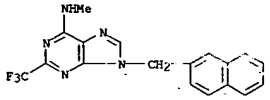


RN 260250-58-6 CAPLUS
CN 9H-Purin-6-amine, N-(2-furanylmethyl)-9-(phenylmethyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

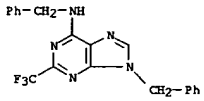


RN 260250-59-7 CAPLUS
CN 9H-Purin-6-amine, N-methyl-9-(2-naphthalenylmethyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

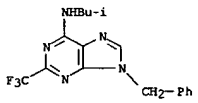
L4 ANSWER 4 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



RN 260250-61-1 CAPLUS
CN 9H-Purin-6-amine, N,9-bis(phenylmethyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

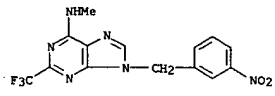


RN 260250-62-2 CAPLUS
CN 9H-Purin-6-amine, N-(2-methylpropyl)-9-(phenylmethyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



IT **260250-43-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of purine derivs. for treatment of liver diseases)

RN 260250-43-9 CAPLUS
CN 9H-Purin-6-amine, N-methyl-9-[(3-nitrophenyl)methyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

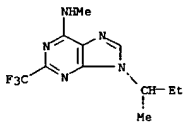


L4 ANSWER 5 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:81353 CAPLUS
DOCUMENT NUMBER: 132:246050
TITLE: Anti-inflammatory activities of a new series of selective phosphodiesterase 4 inhibitors derived from 9-benzyladenine
AUTHOR(S): Boichot, Elisabeth; Wallace, John L.; Germain, Noella; Corbel, Marianne; Lugnier, Claire; Lagente, Vincent; Bourguignon, Jean-Jacques
CORPORATE SOURCE: Institut National de la Sante et de la Recherche Medicale U456, Laboratoire de Pharmacodynamie et de Pharmacologie Moleculaire, Faculte des Sciences Pharmaceutiques et Biologiques, Universite de Rennes 1, Rennes, Fr.
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2000), 292(2), 647-653
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Adenine derivs. substituted in position 9 have been demonstrated to have potent phosphodiesterase (PDE) inhibition properties with high selectivity toward PDE4. We compared the effects of various compds. derived from 9-benzyladenine with those of the selective PDE4 inhibitor RP 73401 on the inhibition of PDE4 isolated from bovine aorta, arachidonic acid, and tumor necrosis factor-.alpha. release by mononuclear cells from healthy subjects. The rank order of potency of the various compds. for in vitro activities on arachidonic acid release is RP 73401 > NCS 613 > NCS 630 > NCS 632 > BWA 78U = NCS 631. The most effective compds. in vitro (RP 73401 and NCS 613) were further investigated in vivo. Both PDE inhibitors dose dependently (1, 10, and 30 mg/kg per os) inhibited the recruitment of neutrophils in the bronchoalveolar lavage fluid of mice exposed to endotoxin via aerosol. Significant differences were obsd. with 10 and 30 mg/kg RP 73401 and 30 mg/kg NCS 613. In rats, RP 73401, but not NCS 613, significantly increased basal acid secretion at 30 mg/kg i.v. and pentagastrin-stimulated acid secretion at 0.3, 1, and 10 mg/kg. These results demonstrate that the compds. derived from 9-benzyladenine, namely NCS 613, elicit anti-inflammatory activities. It is also suggested that their activities have been mediated through the inhibition of PDE4 isoenzyme. The fact that NCS 613 did not stimulate the gastric acid secretion suggests that this compd. may produce fewer gastrointestinal side effects than second-generation PDE4 inhibitors, such as RP 73401.

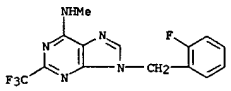
IT **190377-71-0**, NCS 613
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-inflammatory activities of a new series of selective phosphodiesterase 4 inhibitors derived from 9-benzyladenine)
RN 190377-71-0 CAPLUS
CN 9H-Purin-6-amine, 9-[(2-fluorophenyl)methyl]-N-methyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 5 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)

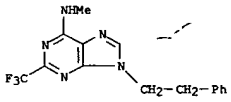


REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

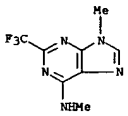
L4 ANSWER 5 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



IT **190377-85-6**, NCS 632 **190377-87-8**, NCS 631
**262383-16-4**, NCS 630
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(anti-inflammatory activities of a new series of selective phosphodiesterase 4 inhibitors derived from 9-benzyladenine)
RN 190377-85-6 CAPLUS
CN 9H-Purin-6-amine, N-methyl-9-(2-phenylethyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 190377-87-8 CAPLUS
CN 9H-Purin-6-amine, N,9-dimethyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

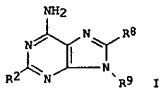


RN 262383-16-4 CAPLUS
CN 9H-Purin-6-amine, N-methyl-9-(1-methylpropyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 6 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:418001 CAPLUS
DOCUMENT NUMBER: 131:68131
TITLE: Adenine derivatives and their pharmaceutical uses
INVENTOR(S): Isobe, Yoshiaki; Ogita, Haruhisa; Tobe, Masanori; Takahisa, Haruo; Matsui, Hiroyuki; Tomisawa, Hideyuki
PATENT ASSIGNEE(S): Japan Energy K. K., Japan; Sumitomo Pharmaceuticals Co., Ltd.
SOURCE: Jpn. Kokai Tokkyo Koho, 16 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 11180982 | A2 | 19990706 | JP 1997-354821 | 19971224 |

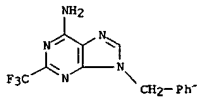
PRIORITY APPLN. INFO.: JP 1997-354821 19971224
OTHER SOURCE(S): MARPAT 131:68131
GI



AB The derivs. I [R2 = CF3, C2F5, Cl; R8 = OH, SH, C.ltoreq.18 acyloxy, C.ltoreq.19 hydrocarbyloxycarbonyloxy; R9 = C.ltoreq.14 hydrocarbyl; in the hydrocarbyl group, CH2 which is not directly bound to the adenine ring may be replaced with CO, SO2, O, S; :CH2 which is not directly bound to the adenine ring may be replaced with O, S; CH of CH3, :CH, :CH2, .tplbond.CH which is not directly bound to the adenine ring may be replaced with N, CX (X = halo), CCN], their tautomers, and their pharmaceutically-acceptable salts are prepd. I, their tautomers, and their salts are useful as interferon secretion stimulants, antiviral agents, anticancer agents, Th2 cell-selective immunosuppressants, allergy inhibitors, and immunomodulators. Title compd. I (R2 = CF3; R8 = OH; R9 = C6H5CH2), 9-benzyl-8-hydroxy-2-trifluoromethyladenine , prepd. from 5-amino-1-benzylimidazole-4-carboxamide with 5 steps, selectively stimulated interferon formation by mouse fibroblast cell line L929 infected with vesicular stomatitis virus. Tablets contg. II were also formulated.

IT **1643-90-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of adenine derivs. as interferon secretion inducers, antiviral and anticancer agents and inflammation inhibitors)
RN 1643-90-9 CAPLUS
CN 9H-Purin-6-amine, 9-(phenylmethyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 6 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)

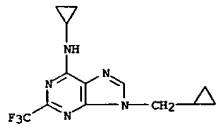


L4 ANSWER 7 OF 47 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:603431 CAPLUS
DOCUMENT NUMBER: 127:248069
TITLE: 6-(Alkylamino)-9-alkylpurines. A New Class of Potential Antipsychotic Agents
AUTHOR(S): Kelley, James L.; Bullock, R. Morris; Krochmal, Mark P.; McLean, Ed W.; Linn, James A.; Durcan, Micheal J.; Cooper, Barrett R.
CORPORATE SOURCE: Division of Organic Chemistry, Burroughs Wellcome Co., Research Triangle Park, NC, 27709, USA
SOURCE: Journal of Medicinal Chemistry (1997), 40(20), 3207-3216
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

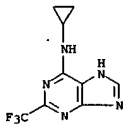
AB A series of 6-(alkylamino)-9-alkylpurines was synthesized and evaluated for the property of antagonizing the behavioral effects in animals of the dopamine agonist apomorphine. This model for identifying potential antipsychotic agents is based on the hypothesis that agents that antagonize apomorphine-induced aggressive behavior in rats and apomorphine-induced climbing in mice, but that do not block stereotyped behavior, could have an antipsychotic effect in humans without producing extrapyramidal side effects. The antiaggressive-behavior activity of the lead compd. [6-(dimethylamino)-9-(3-phenylalaninamidobenzyl)-9H-purine] was improved 48-fold with 6-(cyclopropylamino)-9-(cyclopropylmethyl)-2-(trifluoromethyl)-9H-purine (80) (po ED50 of 2 mg/kg), which was obtained through an iterative sequence of structure-activity relationship studies that encompassed evaluation of the effects of structure variations at the purine 9-, 6-, and 2-positions. Potency was enhanced with a 9-cyclopropyl group, the duration of action was improved with the 6-(cyclopropylamino) substituent, potency was further enhanced with an N-formyl prodrug, and an agent with reduced cardiovascular effect emerged with the 2-trifluoromethyl purine 80. This potential antipsychotic agent was not developed further due to undesirable effects on the stomach.

IT **195252-47-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and antagonism of apomorphine-induced aggression of aminopurines)
RN 195252-47-2 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-(cyclopropylmethyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 7 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)

IT **195252-70-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and antagonism of apomorphine-induced aggression of aminopurines)
RN 195252-70-1 CAPLUS
CN 1H-Purin-6-amine, N-cyclopropyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

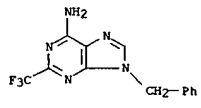


L4 ANSWER 8 OF 47 CAPLUS COPYRIGHT 2003 ACS

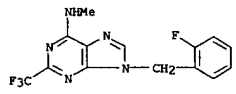
ACCESSION NUMBER: 1997:318282 CAPLUS
DOCUMENT NUMBER: 127:258
TITLE: 9-Benzyladenines: Potent and Selective cAMP Phosphodiesterase Inhibitors
AUTHOR(S): Bourguignon, Jean-Jacques; Desaubry, Laurent; Raboisson, Pierre; Wermuth, Camille-Georges; Lugnier, Claire
CORPORATE SOURCE: Laboratoire de Pharmacochimie Moleculaire, Centre de Neurochimie, Strasbourg, 67084, Fr.
SOURCE: Journal of Medicinal Chemistry (1997), 40(12), 1768-1770
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Among the pharmacol. active adenine derivs., 9-(2-fluorobenzyl)-6-(methylamino)-9H-purine (BWA78U) was found to inhibit the specific cAMP phosphodiesterase (PDE4) with .mu.M range IC50 value. Structural optimization led to a 2-trifluoromethyl adenine deriv. with increased potency and selectivity towards other PDE isoenzymes (IC50 values of 40, 380, 0.04 and 5 .mu.M for PDE1, PDE3, PDE4 and PDE5, resp.).

IT **1643-90-9P 190377-71-0P 190377-85-6P 190377-87-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 9-benzyladenines as cAMP phosphodiesterase inhibitors)
RN 1643-90-9 CAPLUS
CN 9H-Purin-6-amine, 9-(phenylmethyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

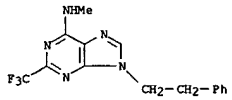


RN 190377-71-0 CAPLUS
CN 9H-Purin-6-amine, 9-[(2-fluorophenyl)methyl]-N-methyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

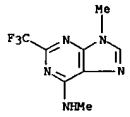


RN 190377-85-6 CAPLUS
CN 9H-Purin-6-amine, N-methyl-9-(2-phenylethyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 8 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)

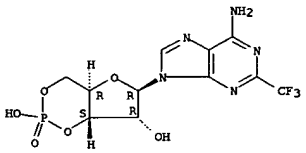


RN 190377-87-8 CAPLUS
CN 9H-Purin-6-amine, N,9-dimethyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



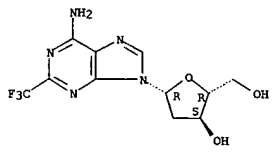
L4 ANSWER 9 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:277755 CAPLUS
DOCUMENT NUMBER: 124:336374
TITLE: QSAR for protein kinase activating cAMP-derivatives with large substituents in positions 2, 6 and 8
AUTHOR(S): Muresan, S.; Bologa, C.; Chiriac, A.; Simon, Z.; Jastorff, B.
CORPORATE SOURCE: Faculty Industrial Chemistry, Technical University Timisoara, Timisoara, 1900, Rom.
SOURCE: Chemical Bulletin of the Technical University of Timisoara (1993), 38(52), 63-75
CODEN: CBTTEH
PUBLISHER: Technical University of Timisoara
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To discern structural characteristics for specific activation of four sites, AI and BI on cAMP-dependent protein kinase-I and AII and BII on cAMP-dependent protein kinase-II, an extended study on a series of cAMP derivs. with large substituents in positions 2, 6 and 8, has been performed. The effect of charged (at pH=7) substituents upon the corresponding receptor affinities has also been investigated.
IT **52940-90-6**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(QSAR for protein kinase activating cAMP-derivs. with large substituents in positions 2, 6 and 8)
RN 52940-90-6 CAPLUS
CN Adenosine, 2-(trifluoromethyl)-, cyclic 3',5'-(hydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



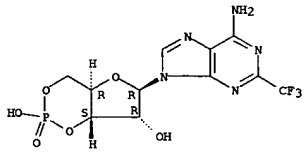
L4 ANSWER 10 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:936459 CAPLUS
DOCUMENT NUMBER: 124:21183
TITLE: Toxicity of adenosine analog against human malaria (Plasmodium falciparum)
AUTHOR(S): Gero, Annette M.; Wood, Andrew M.; Coomber, David W.
CORPORATE SOURCE: School Biochemistry and Molecular Genetics, University New South Wales, Sydney, 2052, Australia
SOURCE: Advances in Experimental Medicine and Biology (1994), 370(Purine and Pyrimidine Metabolism in Man VIII), 487-91
CODEN: AEMBAP; ISSN: 0065-2598
PUBLISHER: Plenum
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Eight of the nucleoside analogs tested were found to be highly toxic to P. falciparum in vitro. Anal. of the purine pools from P. falciparum infected cells incubated with tubercidin suggested that toxic activity may be due to the formation of the di- and tri- nucleotides of tubercidin via the parasite adenosine kinase.
IT **106449-57-4**, Adenosine, 2'-deoxy-2-trifluoromethyl-
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(toxicity of adenosine analog against human malaria (Plasmodium falciparum))
RN 106449-57-4 CAPLUS
CN Adenosine, 2'-deoxy-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 11 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:935087 CAPLUS
DOCUMENT NUMBER: 124:21042
TITLE: Comparative QSAR study with electronic and steric parameters for cAMP derivatives with large substituents in positions 2, 6 and 8
AUTHOR(S): Muresan, S.; Bologa, C.; Mracec, M.; Chiriac, A.; Jastorff, B.; Simon, Z.; Naray-Szabo, G.
CORPORATE SOURCE: Technical University Timisoara, Faculty of Industrial Chemistry, P-ta Victoriei No. 2, Timisoara, RO-1900, Rom.
SOURCE: THEOCHEM (1995), 342, 161-71
CODEN: THEODJ; ISSN: 0166-1280
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In order to discern structural characteristics for specific activation of four sites, AI and BI on cAK-I and AII and BII on cAK-II, an extended study on a series of cAMP derivs. with large substituents in positions 2, 6 and 8, has been performed. The effect of charged (at pH .apprxeq.7) substituents upon the corresponding receptor affinities has also been investigated. The MTD method was used together with the estd. hydrophobicities of the base moiety and the charge on the substituent at the 6-(purinic)-position (calcd. by the AM1 method) as supplementary structural parameters. For the multiparametric correlations, r values between 0.73 and 0.98 were obtained, while in a cross-validation-like procedure, the r 2CV values are between 0.36 and 0.64.
IT **52940-90-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(QSAR study for protein kinase activation of cAMP derivs.)
RN 52940-90-6 CAPLUS
CN Adenosine, 2-(trifluoromethyl)-, cyclic 3',5'-(hydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 12 OF 47 CAPLUS COPYRIGHT 2003 ACS

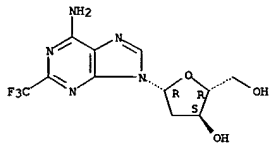
ACCESSION NUMBER: 1994:645191 CAPLUS
DOCUMENT NUMBER: 121:245191
TITLE: Adenosine analogs as antimetabolites against Plasmodium falciparum malaria
AUTHOR(S): Coomber, David W. J.; O'Sullivan, William J.; Gero, Annette M.
CORPORATE SOURCE: School Biochemistry and Molecular Genetics, University New South Wales, Kensington, N.S.W. 2033, Australia
SOURCE: International Journal for Parasitology (1994), 24(3), 357-65
CODEN: IJPYBT; ISSN: 0020-7519
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Analogs of purine nucleosides and deoxynucleosides were tested for toxicity against the intraerythrocytic parasite Plasmodium falciparum in in vitro culture. Sangivamycin (7-deaza-7-amido-adenosine) (IC37 of 0.3 .mu.M), tubercidin (7-deaza-adenosine) (IC37 of 0.7 .mu.M), 6-methylamino-deoxyadenosine (IC37 of 10 .mu.M), 8-aza-2-amino-deoxy-adenosine (IC37 of 11 .mu.M) and 2-chloro-adenosine (IC37 of 11 .mu.M) were found to be the most toxic towards the parasite. Structure-activity anal. suggested that alteration of the purine ring at the 7 or 8 position significantly increased the toxicity of the compd. against P. falciparum. Anal. by HPLC of parasite lysates which had been subjected to the cytotoxic compds. confirmed that alterations in the flux of the purine salvage pathways of the parasite had occurred. Comparison of the toxicity of these compds. against P. falciparum with the toxicity against a similar intraerythrocytic parasite, Babesia bovis, or human melanoma cell lines indicated a differential toxicity, in that many of the compds. toxic towards P. falciparum were relatively non-toxic towards human melanoma cell lines or B. bovis and vice versa. The mechanism of toxicity of the deoxyadenosine and adenosine analogs, whose normal metab. involves transport, metab. and incorporation into nucleic acids appears to vary significantly between P. falciparum, B. bovis and mammalian cells.

IT **106449-57-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adenosine analogs as antimetabolites against Plasmodium falciparum malaria)

RN 106449-57-4 CAPLUS
CN Adenosine, 2'-deoxy-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



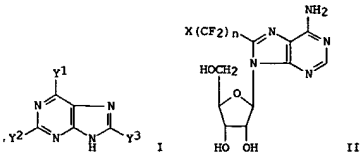
L4 ANSWER 12 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)

L4 ANSWER 13 OF 47 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1993:449145 CAPLUS
DOCUMENT NUMBER: 119:49145
TITLE: Preparation of fluoroalkyl-group containing purine derivatives as carcinostatics and antiviral agents
INVENTOR(S): Nishida, Masakazu; Fujii, Shozo; Kimoto, Hiroshi; Hayakawa, Yoshio; Sawada, Hideo; Mitani, Motohiro; Matsumoto, Takeo; Nakayama, Masaharu
PATENT ASSIGNEE(S): Agency of Industrial Sciences and Technology, Japan; Nippon Oil and Fats Co., Ltd.
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 05001066 | A2 | 19930108 | JP 1991-148912 | 19910620 |
| JP 3086912 | B2 | 20000911 | | |

PRIORITY APPLN. INFO.: JP 1991-148912 19910620
OTHER SOURCE(S): CASREACT 119:49145; MARPAT 119:49145
GI

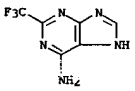


AB The title derivs. I [Y1 = H, OH, (acetyl)amino; Y2 = H, OH, (acetyl)amino, (CF2)nX; Y3 = H, (CF2)nX; Y2 and/or Y3 = (CF3)nX; X = H, F, Cl; n = 1-10] or II, useful as carcinostatics and antiviral agents (no data), are prepd. by treating I (Y3 = H) or adenosine with N,O-bis(trimethylsilyl)trifluoroacetamine (III), followed by X(CF2)nCO2OCO(CF2)nX (IV). A mixt. of adenine, III, pyridine, and ClSiMe3 was heated at 100.degree., the resulting mixt. in CF2ClCFCl2 was treated dropwise with a soln. of IV (X = F, n = 3) in CF2ClCFCl2 at 30.degree. over 1 min, stirring at 30.degree. for 3 h, then refluxed for 1 h to give 11% 8-(perfluoropropyl)adenine and 2% 2-(perfluoropropyl)adenine.

IT **2993-06-8P**, 2-(Trifluoromethyl)adenine
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as carcinostatic and antiviral agent)

RN 2993-06-8 CAPLUS
CN 1H-Purin-6-amine, 2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 13 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



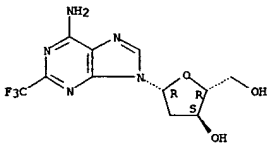
L4 ANSWER 14 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:50895 CAPLUS
DOCUMENT NUMBER: 116:50895
TITLE: The toxicity of adenosine analogs against Babesia bovis in vitro
AUTHOR(S): Kerr, Elizabeth A.; Gero, Annette M.
CORPORATE SOURCE: Sch. Biochem., Univ. New South Wales, Kensington, 2033, Australia
SOURCE: International Journal for Parasitology (1991), 21(6), 747-51
CODEN: IJPYBT; ISSN: 0020-7519
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The toxicity of 20 analogs of deoxyadenosine or adenosine was tested in vitro against the intraerythrocytic parasite Babesia bovis. IC37 values (the concn. of compd. required to reduce cell survival to 37%) were detd. for each compd. Tubercidin (7-deazaadenosine), 2-bromoadenosine, 8-bromo-3-ribosyladenine, and 6-phenylaminodeoxyadenosine were shown to be the most toxic towards B. bovis. Comparison of the toxicity results for these compds. in B. bovis with those in human melanoma cell lines indicated a differential toxicity, in that many of the compds. were toxic towards B. bovis but were relatively nontoxic towards human melanoma cell lines and vice versa. These results suggest that the mechanism of toxicity of the deoxyadenosine and adenosine analogs, whose normal metab. involves transport, metab. and incorporation into nucleic acids, may vary significantly between B. bovis and mammalian cells, allowing such drugs to be considered for parasite chemotherapy.

IT **106449-57-4**
RL: BIOL (Biological study)
(antibabesial activity of, structure in relation to)

RN 106449-57-4 CAPLUS
CN Adenosine, 2'-deoxy-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

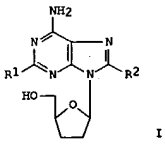
Absolute stereochemistry.



L4 ANSWER 15 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:680484 CAPLUS
DOCUMENT NUMBER: 115:280484
TITLE: Preparation of 8-hydroxy-2',3',-dideoxyadenosine as an antiviral
INVENTOR(S): Nair, Vasu; Buenger, Greg S.
PATENT ASSIGNEE(S): University of Iowa Research Foundation, USA
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 5013829 | A | 19910507 | US 1989-343334 | 19890426 |

PRIORITY APPLN. INFO.: US 1989-343334 19890426
GI



I

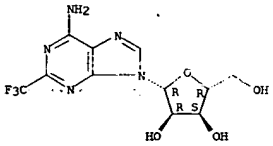
AB Many intermediates [I; R1, R2 = cyano, H; COHN2, H; Et, H, H, OMe; etc.] for the title compd. [I; R1 = H, R2 = OH] (II) stable against deamination and hydrolytic cleavage of the glycosidic bond, an antiviral esp. useful for the treatment of AIDS (no data) were prepd. E.g., a soln. of 8-bromo-2'-deoxyadenosine in MeOH contg. MeONa was refluxed for 20 to give 55% 2'-deoxy-8-methoxyadenosine, which was converted to 2',3'-dideoxy-8-methoxyadenosine via formation of 2'-deoxy-3'-O-(1-imidazolylthiocarbonyl)-5'-O-(tert-butyldimethylsilyl)adenosine, deoxygenation, and desilylation (detailed procedures not given). The conversion into II is not illustrated.

IT **4627-40-1P 122970-33-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for stable antivirals)

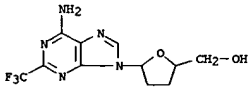
RN 4627-40-1 CAPLUS
CN Adenosine, 2-(trifluoromethyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 15 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



RN 122970-33-6 CAPLUS
CN Adenosine, 2',3'-dideoxy-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

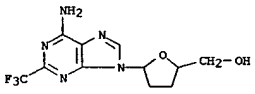


L4 ANSWER 16 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:484886 CAPLUS
DOCUMENT NUMBER: 115:84886
TITLE: Inhibition of mammalian adenosine deaminase by novel functionalized 2',3'-dideoxyadenosines
AUTHOR(S): Nair, Vasu; Buenger, Greg S.; Sells, Todd B.
CORPORATE SOURCE: Dep. Chem., Univ. Iowa, Iowa City, IA, 52242, USA
SOURCE: Biochimica et Biophysica Acta (1991), 1078(1), 121-3
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English

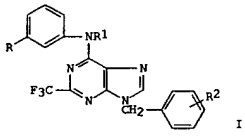
AB 2',3'-Dideoxyadenosine analogs with a variety of functionalization at the 2-position, previously synthesized by a combination of thermal, photochem. and metal-mediated methodologies, were either totally resistant to deamination by mammalian adenosine deaminase (ADA) or were very poor substrates of ADA. They were competitive inhibitors of this enzyme.

IT **122970-33-6**
RL: BIOL (Biological study)
(adenosine deaminase inhibition by)

RN 122970-33-6 CAPLUS
CN Adenosine, 2',3'-dideoxy-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 17 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1991:81380 CAPLUS
DOCUMENT NUMBER: 114:81380
TITLE: 6-(3-Fluoroanilino)-9-(substituted-benzyl)-2-trifluoromethyl-9H-purines with antirhinovirus activity
AUTHOR(S): Kelley, J. L.; Linn, J. A.; Davis, R. G.; Selway, J. W. T.
CORPORATE SOURCE: Div. Org. Chem., Burroughs Wellcome Co., Research Triangle Park, NC, 27709, USA
SOURCE: European Journal of Medicinal Chemistry (1990), 25(7), 623-8
CODEN: EJMCA5; ISSN: 0223-5234
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:81380
GI

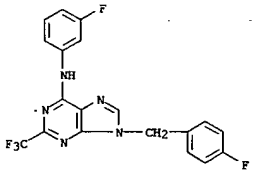


I

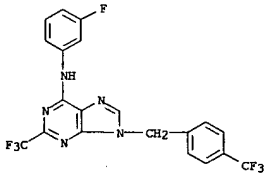
AB Title compds. I (R = H, F; R1 = H, Me, Et; R2 = H, 4-Me, 4-F, 4-CF3, 4-NMe2, 4-NH2, 4-cyano, 4-NO2, 3-F, 2-F) were prepd. by alkylation of a 6-anilino-2-trifluoromethylpurine with a benzyl halide or by amination of a 6-chloro-9-benzylpurine with an aniline. I had activity against rhinovirus serotype 1B. I (R = F, R1 = H, R2 = 3-F) had good activity (ED50 = 0.4-13 .mu.M) against 80% of the 47 serotypes tested, but pharmacokinetic studies indicated poor oral bioavailability.
IT **132000-56-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and benzylation of)
RN 132000-56-7 CAPLUS
CN 1H-Purin-6-amine, N-(3-fluorophenyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 17 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)

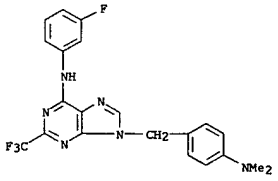
RN 132000-45-4 CAPLUS
CN 9H-Purin-6-amine, N-(3-fluorophenyl)-9-[(4-fluorophenyl)methyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 132000-46-5 CAPLUS
CN 9H-Purin-6-amine, N-(3-fluorophenyl)-2-(trifluoromethyl)-9-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

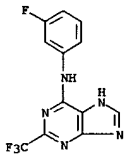


RN 132000-47-6 CAPLUS
CN 9H-Purin-6-amine, 9-[[4-(dimethylamino)phenyl]methyl]-N-(3-fluorophenyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

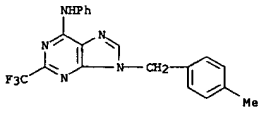


RN 132000-48-7 CAPLUS

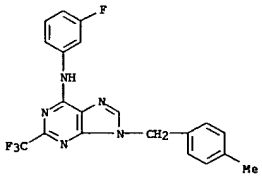
L4 ANSWER 17 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



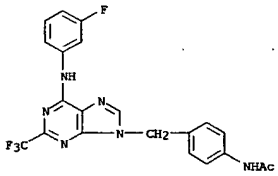
IT **132000-42-1P 132000-44-3P 132000-45-4P**
**132000-46-5P 132000-47-6P 132000-48-7P**
**132000-49-8P 132000-50-1P 132000-51-2P**
**132000-52-3P 132000-53-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and virucidal activity of)
RN 132000-42-1 CAPLUS
CN 9H-Purin-6-amine, 9-[(4-methylphenyl)methyl]-N-phenyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



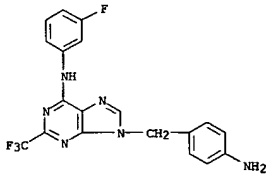
RN 132000-44-3 CAPLUS
CN 9H-Purin-6-amine, N-(3-fluorophenyl)-9-[(4-methylphenyl)methyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



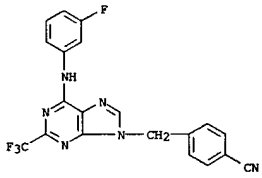
L4 ANSWER 17 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)
CN Acetamide, N-[4-[[6-[(3-fluorophenyl)amino]-2-(trifluoromethyl)-9H-purin-9-yl]methyl]phenyl]- (9CI) (CA INDEX NAME)



RN 132000-49-8 CAPLUS
CN 9H-Purin-6-amine, 9-[(4-aminophenyl)methyl]-N-(3-fluorophenyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

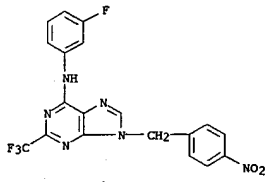


RN 132000-50-1 CAPLUS
CN Benzonitrile, 4-[[6-[(3-fluorophenyl)amino]-2-(trifluoromethyl)-9H-purin-9-yl]methyl]- (9CI) (CA INDEX NAME)

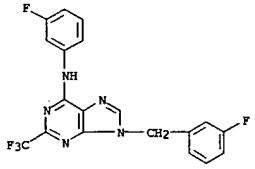


RN 132000-51-2 CAPLUS
CN 9H-Purin-6-amine, N-(3-fluorophenyl)-9-[(4-nitrophenyl)methyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

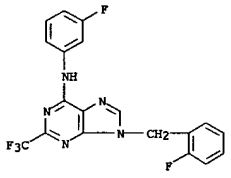
L4 ANSWER 17 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



RN 132000-52-3 CAPLUS
CN 9H-Purin-6-amine, N-(3-fluorophenyl)-9-[(3-fluorophenyl)methyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 132000-53-4 CAPLUS
CN 9H-Purin-6-amine, N-(3-fluorophenyl)-9-[(2-fluorophenyl)methyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 18 OF 47 CAPLUS COPYRIGHT 2003 ACS

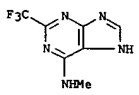
ACCESSION NUMBER: 1991:61810 CAPLUS
DOCUMENT NUMBER: 114:61810
TITLE: 8-Bromo-6-(alkylamino)-2-trifluoromethyl-9H-purines with in vitro activity against influenza A virus
AUTHOR(S): Kelley, James L.; Linn, James A.; Tisdale, Margaret
CORPORATE SOURCE: Div. Org. Chem., Burroughs Wellcome Co., Research Triangle Park, NC, 27709, USA
SOURCE: Journal of Heterocyclic Chemistry (1990), 27(5), 1505-8
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

I

AB Several derivs. of 8-bromo-6-dimethylamino-2-trifluoromethyl-9H-purine (I, R = H, Me, Et, Pr, cyclopropyl, CH2Ph) and some analogs were synthesized for structure-activity relationship studies of anti-influenza A virus activity. I were prepd. by reaction of the anion of the 6-alkylamino-2-trifluoromethylpurines with N-bromosuccinimide. Several compds. had in vitro antiinfluenza activity comparable to ribavirin, but no in vivo activity was obsd.

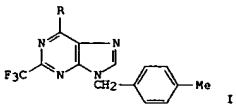
IT **18925-07-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and bromination of)

RN 18925-07-0 CAPLUS
CN 1H-Purin-6-amine, N-methyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 19 OF 47 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1990:497315 CAPLUS
DOCUMENT NUMBER: 113:97315
TITLE: Antirhinovirus structure-activity relationships of 6-substituted-9-(4-methylbenzyl)-2-trifluoromethyl-9H-purines
AUTHOR(S): Kelley, James L.; Linn, James A.; Selway, J. W. T.
CORPORATE SOURCE: Div. Org. Chem., Burroughs Wellcome Co., Research Triangle Park, NC, 27709, USA
SOURCE: European Journal of Medicinal Chemistry (1990), 25(2), 131-5
CODEN: EJMCA5; ISSN: 0223-5234
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 113:97315
GI

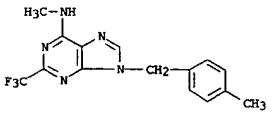


I

AB To evaluate the effect of different 6-substituents on antirhinoviral activity, a series of title compds. I (R = NH2, NMeR1, H, OH, OMe, SMe; R1 = H, alkyl, Ph, OH, OMe, Ac) was synthesized and tested. A matrix map of space adjacent to the 6-position was constructed to facilitate structure-activity anal. This study provided evidence that a lipophilic pocket exists on the virus capsid surface, which accommodates the Me group of I (R = NMeR1).

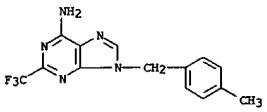
IT **128838-20-0P 128838-21-1P 128838-27-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and virucidal activity of, against rhinovirus)

RN 128838-20-0 CAPLUS
CN 9H-Purin-6-amine, N-methyl-9-[(4-methylphenyl)methyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

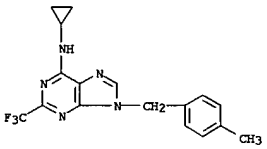


RN 128838-21-1 CAPLUS
CN 9H-Purin-6-amine, 9-[(4-methylphenyl)methyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

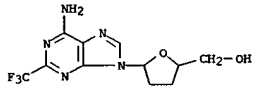
L4 ANSWER 19 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



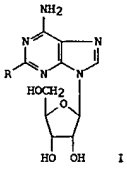
RN 128838-27-7 CAPLUS
CN 9H-Purin-6-amine, N-cyclopropyl-9-[(4-methylphenyl)methyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 20 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1990:406736 CAPLUS
DOCUMENT NUMBER: 113:6736
TITLE: Hydrolysis of dideoxygenated purine nucleosides: effect of modification of the base moiety
AUTHOR(S): Nair, Vasu; Buenger, Greg S.
CORPORATE SOURCE: Dep. Chem., Univ. Iowa, Iowa City, IA, 52242, USA
SOURCE: Journal of Organic Chemistry (1990), 55(11), 3695-7
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The rates of acid-catalyzed glycosidic bond hydrolysis of fourteen analogs of the anti-HIV compd., 2',3'-dideoxyadenosine (ddA), were studied. Substitution at the 2-position of ddA resulted in increased stability. While removal of the amino group from the 6-position decreased stability, its transposition to the 2-position resulted in little change in the hydrolysis rate. The most dramatic effects came from substitution at the 8-position. These studies pont to the importance of protonation of N(7) for facile hydrolysis of dideoxynucleosides.
IT 122970-33-6
RL: PRP (Properties)
(hydrolysis of glycosidic bond of, structure of base moiety in relation to)
RN 122970-33-6 CAPLUS
CN Adenosine, 2',3'-dideoxy-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



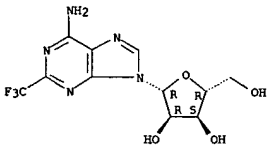
L4 ANSWER 21 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1990:119289 CAPLUS
DOCUMENT NUMBER: 112:119289
TITLE: Synthesis of congeners of adenosine resistant to deamination by adenosine deaminase
AUTHOR(S): Nair, Vasu; Purdy, David F.; Sells, Todd B.
CORPORATE SOURCE: Dep. Chem., Univ. Iowa, Iowa City, IA, 52242, USA
SOURCE: Journal of the Chemical Society, Chemical Communications (1989), (13), 878-9
CODEN: JCCCAT; ISSN: 0022-4936
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 112:119289
GI



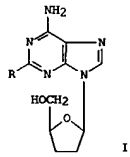
I

AB The metal-mediated prepn. of deaminase resistant adenosine congeners I [R = CH2:CH, HOCH2CH(OH), Et, F3C, cyano] from I (R = iodo) is described.
IT 4627-40-1P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and resistance of, to deamination by adenosine deaminase)
RN 4627-40-1 CAPLUS
CN Adenosine, 2-(trifluoromethyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



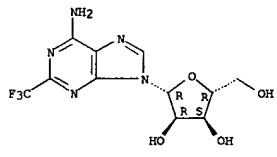
L4 ANSWER 22 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1989:574576 CAPLUS
DOCUMENT NUMBER: 111:174576
TITLE: Novel, stable congeners of the antiretroviral compound 2',3'-dideoxyadenosine
AUTHOR(S): Nair, Vasu; Buenger, Greg S.
CORPORATE SOURCE: Dep. Chem., Univ. Iowa, Iowa City, IA, 52242, USA
SOURCE: Journal of the American Chemical Society (1989), 111(22), 8502-4
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 111:174576
GI



I

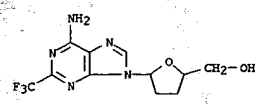
AB Novel congeners I (R = cyano, Et, SMe, iodo, CF3) and the 2',3'-didehydro analog of I (R = cyano) of the antiretroviral compd. 2',3'-dideoxyadenosine (I, R = H) have been synthesized through metal-mediated and photochem. conversions as the key steps. These compds. are inherently more stable than I (R = H) with respect to both glycosidic bond cleavage and deamination by adenosine deaminase.
IT 4627-40-1P, 2-Trifluoromethyladenosine
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and conversion of, to dideoxy deriv.)
RN 4627-40-1 CAPLUS
CN Adenosine, 2-(trifluoromethyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 122970-33-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 122970-33-6 CAPLUS

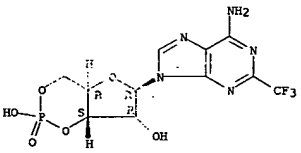
L4 ANSWER 22 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)
CN Adenosine, 2',3'-dideoxy-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 23 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1989:227690 CAPLUS
DOCUMENT NUMBER: 110:227690
TITLE: Comparison of the two classes of binding sites (A and B) of type I and type II cyclic-AMP-dependent protein kinases by using cyclic nucleotide analogs
AUTHOR(S): Oegreid, Dagfinn; Ekanger, Roald; Suva, Robert H.; Miller, Jon P.; Doskeland, Stein Ove
CORPORATE SOURCE: Inst. Anat., Univ. Bergen, Bergen, N-5009, Norway
SOURCE: European Journal of Biochemistry (1989), 181(1), 19-31
CODEN: EJBCAI; ISSN: 0014-2956
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Analogs of cAMP, all 96 of which were modified in the adenine moiety, were examd. quant. for their ability to inhibit the binding of [3H]cAMP to each of the 2 classes (A and B) of cAMP-binding sites of type I (rabbit skeletal muscle) and type II (bovine heart) cAMP-dependent protein kinase. The study showed that analogs can be constructed that have a higher affinity than cAMP for a binding site. N6-Phenyl-cAMP had 18-fold increased affinity for site A or RI (AI) and 40-fold increased for site AII. 2-Chloro-8-methylamino-cAMP had a 7-fold increased affinity for BI, and 8-(4-chlorophenylthio)-cAMP had 17-fold increased affinity for BII. Analogs could discriminate between the 2 classes of binding sites by >2 orders of magnitude in binding affinity: 2-chloro-8-methylamino-cAMP had 170-fold higher affinity for BI than for AI, and 2-n-butyl-8-thiobenzyl-cAMP had 700-fold higher affinity for BII than for AII. Analogs could also discriminate between the homologous binding sites of the isoenzymes; 2-n-butyl-8-bromo-cAMP had 260-fold higher affinity for AI than for AII (22-fold higher for BII than BI), and 8-piperidino-cAMP had 50-fold higher affinity for BII than for BI (and 50-fold higher for AI than for AII). The data suggest the following conclusions. Stacking interactions are important for the binding of cAMP to all the binding sites. Subtle differences exist between the sites as to the optimal electron distribution in the adenine ring since modifications that withdraw electrons at C2 and donate at C8 favor binding to BI, and disfavor binding to AI and AII. There are no H bonds between the adenine ring of cAMP and any of the binding sites. All sites bind cAMP in the syn conformation. The subsites adjacent to the N6 and C8 positions may have nonpolar neighboring regions since hydrophobic substituents at N6 could increase the affinity for AI and AII and similar substituents at C8 could increase the affinity for BII. Finally, the sites differed in their ability to accommodate bulky substituents at C2 and c8. For all compds. tested, their potency as activators of protein kinases I and II correlated, in a predictable fashion, to their mean affinity for the 2 classes of binding sites, rather than to the affinity for only one of the sites.
IT **52940-90-6**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(cAMP-dependent protein kinases types I and II multiple sites binding and activation by, structure in relation to)
RN 52940-90-6 CAPLUS
CN Adenosine, 2-(trifluoromethyl)-, cyclic 3',5'-(hydrogen phosphate) (9CI) (CA INDEX NAME)

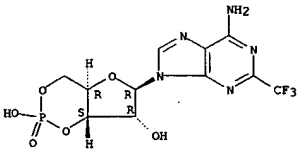
Absolute stereochemistry.

L4 ANSWER 23 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



L4 ANSWER 24 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1989:20319 CAPLUS
DOCUMENT NUMBER: 110:20319
TITLE: cAMP analogs used to study low-Km, hormone-sensitive phosphodiesterase
AUTHOR(S): Beebe, Stephen J.; Beasley-Leach, Alfreda; Corbin, Jackie D.
CORPORATE SOURCE: Inst. Pathol., Rikshosp., Oslo, Norway
SOURCE: Methods in Enzymology (1988), 159(Initiation Termination Cyclic Nucleotide Action), 531-40
CODEN: MENZAU; ISSN: 0076-6879
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Using more than 30 cyclic nucleotide analogs, a method is described to det. specificities for phosphodiesterase. Since most analogs are not available with radioactive labels, the analogs are tested by inhibition of [3H]cAMP hydrolysis. Comparisons are made using I50 values which is defined as the conc. of analog required to inhibit [3H]cAMP hydrolysis by 50%. The low-Km, hormone-sensitive phosphodiesterases from adipocyte and hepatocyte (type IV) are used as models to illustrate the method.
IT **52940-90-6**, 2-Trifluoromethyl-cAMP
RL: BIOL (Biological study)
(cAMP phosphodiesterase of adipocyte and hepatocyte inhibition by)
RN 52940-90-6 CAPLUS
CN Adenosine, 2-(trifluoromethyl)-, cyclic 3',5'-(hydrogen phosphate) (9CI) (CA INDEX NAME)

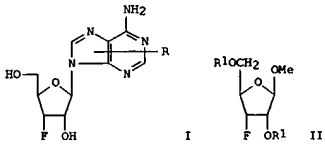
Absolute stereochemistry.



L4 ANSWER 25 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1988:406901 CAPLUS
DOCUMENT NUMBER: 109:6901
TITLE: Preparation of fluoroadenosine derivatives as antitumor agents
INVENTOR(S): Sasaki, Takuma; Uchida, Keiichi; Yasuda, Arata; Morisawa, Yoshitomi
PATENT ASSIGNEE(S): Asahi Glass Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 62240622 | A2 | 19871021 | JP 1986-82317 | 19860411 |

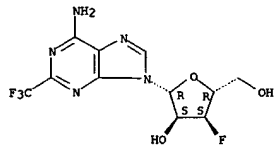
PRIORITY APPLN. INFO.: JP 1986-82317 19860411
OTHER SOURCE(S): CASREACT 109:6901
GI



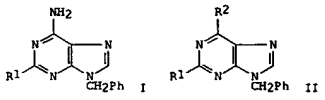
AB The title compds. I (R = H, halo, CF3 at positions 2 and 8 on adenine ring), useful as antitumor agents, are prepd. Treatment of II (R1 = PhCO) with 30% HBr-AcOH soln., followed successively by reaction of the crude product with adenine monobenzoate in the presence of Hg(CN)2 and heating in MeOH contg. MeONa, gave 9-(3-deoxy-3-fluoro-.beta.-D-ribofuranosyl)adenine (III). At 3 .mu.g/mL, III in vitro inhibited mouse leukemia (L 5178Y) cells by 96.8%.
IT **114752-63-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as antitumor agent)
RN 114752-63-5 CAPLUS
CN Adenosine, 3'-deoxy-3'-fluoro-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

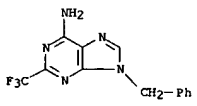
L4 ANSWER 25 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



L4 ANSWER 26 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1988:75095 CAPLUS
DOCUMENT NUMBER: 108:75095
TITLE: The Gomberg-Bachmann reaction of purines
AUTHOR(S): McKenzie, Thomas C.; Rolfes, Steven M.
CORPORATE SOURCE: Chem. Dep., Univ. Alabama, Tuscaloosa, AL, 35487, USA
SOURCE: Journal of Heterocyclic Chemistry (1987), 24(3), 659-61
CODEN: JHTCAD; ISSN: 0022-152X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 108:75095
GI



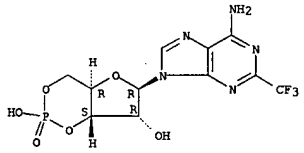
AB Adenines I (R1 = OMe, CF3) were treated with isoamyl nitrite and C6H6 and PhOMe to give arylated products II (R2 = Ph, anisyl).
IT **1643-90-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(Gomberg-Bachmann coupling reaction of, with isoamyl nitrite and benzene and anisole)
RN 1643-90-9 CAPLUS
CN 9H-Purin-6-amine, 9-(phenylmethyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 27 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1987:511652 CAPLUS
DOCUMENT NUMBER: 107:111652
TITLE: Characterization of the cyclic adenosine 3':5'-monophosphate effector system in hormone-dependent and hormone-independent rat mammary carcinomas
AUTHOR(S): Engegrein, Dagfinn; Yoon, Sang Cho Chung; Ekanger, Roald; Vinterwyl, Olav; Haarstad, Jan; Doeskeland, Stein Ove
CORPORATE SOURCE: Inst. Anat., Univ. Bergen, Bergen, N-5000, Norway
SOURCE: Cancer Research (1987), 47(10), 2576-82
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The properties of cAMP-dependent protein kinases I and II in hormone-dependent/cAMP-sensitive [DMBA (7,12-dimethyl benz(a)anthracene) tumor] and hormone-independent/cAMP-resistant (DMBA 1 tumor) rat mammary carcinomas. The cAMP-resistance was not due to (1) less total kinase in the hormone-independent tumor, (2) grossly altered distribution between sol. and particulate forms of the kinase (80% sol. in either tumor), (3) alteration in the relative proportion of isoenzymes I and II of the protein kinase (the sol. and the particulate fraction from both tumors contained .apprx.50% of either isoenzyme), or (4) a decreased sensitivity toward cAMP (both isoenzymes had affinities for cAMP and its derivs. that corresponded closely with those of isoenzymes from normal tissues). Furthermore, the sensitivity of the enzymes towards thermal denaturation was identical for samples from the 2 tumor types. Subtle differences did, however, exist between the regulatory moieties [regulatory subunit of cAMP-dependent protein kinase II (RII)] of isoenzyme II from the 2 tumors: (1) autophosphorylated RII from the hormone-independent tumor migrated as a doublet corresponding to mol. wt., 54,000 and 52,000 on SDS-polyacrylamide gels, compared to mol. wt. 53,000 and 52,000 for RII from the hormone-dependent tumor; (2) RII from the 2 tumors showed different elution profiles upon DEAE-cellulose chromatog.; (3) a considerable proportion of the sol. RII in the hormone-independent tumor formed supramol. aggregates as judged by size-exclusion chromatog. No such microheterogeneity was noted for isoenzyme I. This study thus shows that the lack of cAMP-responsiveness of one tumor is related either to a defect distal to the cAMP-dependent protein kinases or to the appearance of the new subtype of RII in the resistant tumor. If the latter explanation is correct, it means that the part of the RII mol. responsible for interaction with other proteins rather than that responsible for cAMP-binding and control of protein kinase activity modulates the growth-inhibition response to cAMP.
IT **52940-90-6**
RL: BIOL (Biological study)
(protein kinase isoenzymes of hormone-dependent and -independent mammary carcinoma affinity for)
RN 52940-90-6 CAPLUS
CN Adenosine, 2-(trifluoromethyl)-, cyclic 3',5'-(hydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 27 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



L4 ANSWER 28 OF 47 CAPLUS COPYRIGHT 2003 ACS

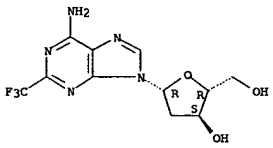
ACCESSION NUMBER: 1987:60777 CAPLUS
DOCUMENT NUMBER: 106:60777
TITLE: Selective toxicity of deoxyadenosine analogs in human melanoma cell lines
AUTHOR(S): Parsons, P. G.; Bowman, E. P. W.; Blakley, R. L.
CORPORATE SOURCE: Queensland Inst. Med. Res., Herston, 4006, Australia
SOURCE: Biochemical Pharmacology (1986), 35(22), 4025-9
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The in vitro toxicities of 19 analogs of deoxyadenosine were tested, using a panel of human melanoma cell lines including 2 lines sensitive to deoxyadenosine [958-09-8] and deoxyinosine [890-38-0]. The 2-fluoro- [21679-12-9], 2-chloro [4291-63-8], 2-bromo- [89178-21-2] and 2-amino-8-aza deriv. [37113-44-3] were the most toxic and showed selectivity against deoxyadenosine-sensitive cells. 2-Bromodeoxyadenosine (BrdAdo) and its 5'-phosphate [106449-55-2] were less potent than the chloro compd. but showed the greatest selectivity. In further studies of BrdAdo, a 3rd sensitive melanoma line was identified of the 8 tested. A treatment time of 24 h or more was required to develop toxicity to BrAdo; this could be prevented by deoxycytidine [951-77-9] or cytidine [65-46-3] added to the medium but not by other nucleosides. Flow cytometry showed that BrdAdo blocked cells in the G1 and S phases of the cell cycle. DNA synthesis as judged by thymidine incorporation was rapidly inhibited by BrdAdo to an extent which reflected the sensitivity of the particular cell line; RNA synthesis was less affected. Exposure to BrdAdo for 48 h induced breaks in the preformed DNA of sensitive but not resistant cells. The toxicity of BrdAdo is assocd. with prolonged inhibition of DNA synthesis and subsequent DNA fragmentation.

IT **106449-57-4**
RL: BIOL (Biological study)
(melanoma of humans response to)

RN 106449-57-4 CAPLUS
CN Adenosine, 2'-deoxy-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 29 OF 47 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1987:30526 CAPLUS
DOCUMENT NUMBER: 106:30526
TITLE: The use of cAMP analogs to study cAMP-dependent protein kinase-mediated events in intact mammalian cells
AUTHOR(S): Beebe, S. J.; Blackmore, P. F.; Segaloff, D. L.; Koch, S. R.; Burks, D.; Limbird, L. E.; Granner, D. K.; Corbin, J. D.
CORPORATE SOURCE: Med. Cent., Vanderbilt Univ., Nashville, TN, 37232, USA
SOURCE: Colloque INSERM (1986), 139(Horm. Cell Regul.), 159-80
CODEN: CINMDE; ISSN: 0768-3154
DOCUMENT TYPE: Journal
LANGUAGE: English

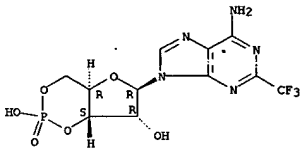
AB cAMP analogs were used in several intact mammalian cell prepns. to study physiol. responses mediated by the cAMP-dependent protein kinase (cA PK). These included adipocyte lipolysis, hepatocyte glycogenolysis, H4 hepatoma cell phosphoenolpyruvate carboxykinase gene transcription, and granulosa cell LH receptor induction and progesterone synthesis. The basic principles which detd. the efficacy of the analogs in stimulating these responses were: the partitioning characteristic of the analog, the concn. of analog required for protein kinase activation in vitro, and the susceptibility of the analogs to hydrolysis by phosphodiesterases. The efficacy of the analogs differed among the various cell types. For example, hepatocyte glycogenolysis was 100-10,000 times more sensitive to analog stimulation than was adipocyte lipolysis. To det. if cA PK was responsible for a cAMP effect, advantage was taken of a unique property of cA PK. The cA PK can be synergistically activated in vitro and in vivo by using pairs of cAMP analogs, each one selective for one or the other of 2 intrasubunit cAMP binding sites (Site 1 and Site 2) on cA PK. Various Site 1- and Site 2-selective analogs were added alone (in the linear dose-response range) and in combination, both in vitro to Type I and(or) Type II cA PK isolated from various cell types, and to intact cells. Correlations were then made between the extent of synergism of cA PK activation and the synergism of the various physiol. responses. All analog pairs which resulted in a synergistic activation of the resp. cA PKs resulted in a synergistic increase in all the resp. intact cell responses mentioned above. For all responses tested, synergism occurred only when Site 1- and Site 2-selective analogs were combined, a cA PK-specific characteristic. Because the synergism of cA PK, activation was strongly correlated with the synergism of the intact cell responses. CA PK could be entirely responsible for the cAMP activation of all the physiol. responses tested.

IT **52940-90-6**, 2-Trifluoromethyl-cAMP
RL: BIOL (Biological study)
(protein kinase function response to, in mammalian cells)

RN 52940-90-6 CAPLUS
CN Adenosine, 2-(trifluoromethyl)-, cyclic 3',5'-(hydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

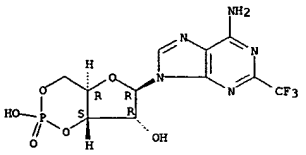
L4 ANSWER 29 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



L4 ANSWER 30 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1985:418907 CAPLUS
DOCUMENT NUMBER: 103:18907
TITLE: Activation of protein kinase isozymes by cyclic nucleotide analogs used singly or in combination. Principles for optimizing the isozyme specificity of analog combinations
AUTHOR(S): Ogreid, Dagfinn; Ekanger, Roald; Suva, Robert H.; Miller, Jon P.; Sturm, Priscilla; Corbin, Jackie D.; Doeskeland, Stein Ove
CORPORATE SOURCE: Dep. Anat., Univ. Bergen, Bergen, N-5000, Norway
SOURCE: European Journal of Biochemistry (1985), 150(1), 219-27
CODEN: EJBCAI; ISSN: 0014-2956
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A large no. (104) of cAMP analogs, most of them modified in the adenine moiety, were tested as activators of cAMP-dependent protein kinase I (from rabbit or rat skeletal muscle) and kinase II (from bovine heart or rat skeletal muscle). When tested singly, only 2-phenyl-1,N6-etheno-cAMP showed a considerably (7-fold) higher potency as an activator of kinase II than of kinase I. Analogs contg. an 8-amino modification preferentially activated kinase I, some being >10-fold more potent as activators of kinase I than kinase II. When 2 analogs were combined, the concn. of 1 (complementary) analog required to activate half-maximally each isoenzyme was detd. in the presence of a fixed concn. of another (priming) analog. Analogs tested in combination were analyzed for their affinity for the intrasubunit binding sites (A,B) of isoenzyme I and II. The degree to which complementary analogs preferentially activated 1 isoenzyme was plotted against the mean site selectivity. This plot produced a straight line, the slope of which reflected the ability of the priming analog to discriminate homologous sites on the isoenzymes. Thus, the isoenzyme-discriminating power of an analog pair can be quant. predicted from the affinity of the analogs for site A and B of the 2 enzymes and a systematic anal. of those features of analogs imparting a high mean site selectivity or the ability to discriminate between homologous isoenzyme sites will facilitate the synthesis of addnl. even more isoenzyme-selective analogs.
IT **52940-90-6**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(protein kinase isoenzymes activation by, specificity of)
RN 52940-90-6 CAPLUS
CN Adenosine, 2-(trifluoromethyl)-, cyclic 3',5'-(hydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

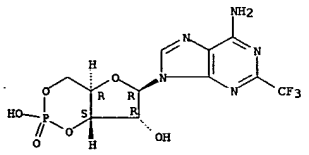
L4 ANSWER 30 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



L4 ANSWER 31 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1984:468256 CAPLUS
DOCUMENT NUMBER: 101:68256
TITLE: Rat adipose tissue cAMP-dependent protein kinase: a unique form of type II
AUTHOR(S): Beebe, Stephen J.; Corbin, Jackie D.
CORPORATE SOURCE: Med. Sch., Vanderbilt Univ., Nashville, TN, 37232, USA
SOURCE: Molecular and Cellular Endocrinology (1984), 38(1-2), 67-78
CODEN: MCEND6; ISSN: 0303-7207
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The rat adipose tissue cAMP-dependent protein kinase type II holoenzyme (type II) and regulatory (R) subunit were compared with type II from bovine heart and several other species and tissues. Adipose tissue type II was similar to the bovine heart type II by several criteria (S20.w = 7.0, similar site 1 and site 2 dissocn. rates for [3H]cAMP, rapid autophosphorylation, and lack of MgATP inhibition of [3H]cAMP binding). However, some of its phys. characteristics were similar to protein kinase type I (type I). The apparent mol. wt. (detd. by SDS-gel electrophoresis) of the homogeneous adipose tissue R subunit was 51,000 daltons, compared to 49,000 for type I and 53,000-58,000 for other type II R subunits. The adipose tissue holoenzyme eluted from DEAE-cellulose at an intermediate position between type I and bovine heart type II. The adipose tissue and bovine heart holoenzymes differed in several properties, including Stokes radius (5.2 nm vs. 6.0 nm), calcd. mol. wt. (157,000 vs. 181,000 daltons), and frictional ratio (1.47 vs. 1.60). After autophosphorylation, the adipose tissue R subunit, like type IIB forms from other species and tissues, did not shift to a higher apparent mol. wt. on SDS-gel electrophoresis, in contrast to bovine heart type IIR subunit (a type IIA form). Even though the adipose tissue enzyme was quite similar to other type II forms in the kinetics of cAMP action, its cAMP-binding sites were differentiated from those of the other type II forms by the use of cAMP analogs. The apparent Ka values (the concn. of cyclic nucleotide required for half-maximal enzyme activation) for cAMP analogs modified at the N6 position of the adenine ring, such as N6-benzoyl-cAMP, were higher in protein kinase of adipose tissue than in the bovine and several other heart isozymes. The cAMP analogs modified at the 8 C atom of the adenine ring showed pos. cooperativity of activation for the adipose tissue enzyme, but not for the bovine heart holoenzyme. The adipose tissue isozyme is the 1st type II form described to have a distinct kinetic characteristic.
IT **52940-90-6**
RL: BIOL (Biological study)
(protein kinase type II of adipose tissue and heart activation by, cooperativity in relation to)
RN 52940-90-6 CAPLUS
CN Adenosine, 2-(trifluoromethyl)-, cyclic 3',5'-(hydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

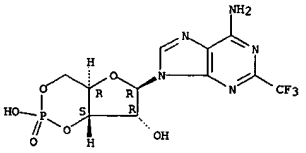
L4 ANSWER 31 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



L4 ANSWER 32 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1984:185330 CAPLUS
DOCUMENT NUMBER: 100:185330
TITLE: Two classes of cAMP analogs which are selective for the two different cAMP-binding sites of type II protein kinase demonstrate synergism when added together to intact adipocytes
AUTHOR(S): Beebe, Stephen J.; Holloway, Rob; Rannels, Stephen R.; Corbin, Jackie D.
CORPORATE SOURCE: Sch. Med., Vanderbilt Univ., Nashville, TN, 37232, USA
SOURCE: Journal of Biological Chemistry (1984), 259(6), 3539-47
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several cyclic nucleotide analogs were tested individually to act as lipolytic agents and to activate adipocyte protein kinase [9026-43-1]. The lipolytic potency of individual analogs correlated better with their Ka for protein kinase and their lipophilicity rather than with either parameter alone. Some of the most potent lipolytic analogs had high ID50 values for the particulate low Km cAMP phosphodiesterase suggesting that their effect was not due to raising endogenous cAMP levels through inhibition of phosphodiesterase. The most potent lipolytic analogs contained a thio moiety at the C-8 or C-6 position. These analogs exhibited concave upward dose-response curves. At high concns., some analogs were as effective as optimal concns. of epinephrine in stimulating glycerol release. The regulatory subunit of protein kinase has 2 different intrachain cAMP-binding sites and cAMP analogs modified at the C-8 position (C-8 analogs) are generally selective for site 1 and analogs modified at the C-6 position (C-6 analogs) are generally selective for site 2. Thus, C-8 and C-6 analogs were tested in combination to stimulate lipolysis in intact adipocytes and to activate protein kinase in vitro. Each process was stimulated synergistically by a combination of a C-6 and C-8 analog. Two C-8 analogs or 2 C-6 analogs added together did not cause synergism of either process. For both lipolysis and protein kinase activation, C-8 thio analogs acted more synergistically than C-8 amino analogs when incubated in combination with C-6 analogs, a characteristic of type II protein kinase. Thus, the obsd. synergism of lipolysis is due to binding of cAMP analogs to both intrachain sites. The type II protein kinase isozyme appears to be responsible for the lipolytic response.
IT **52940-90-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(lipolytic activity of, in adipocytes, protein kinase binding in relation to)
RN 52940-90-6 CAPLUS
CN Adenosine, 2-(trifluoromethyl)-, cyclic 3',5'-(hydrogen phosphate) (9CI) (CA INDEX NAME)

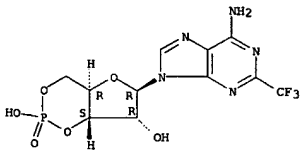
Absolute stereochemistry.

L4 ANSWER 32 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



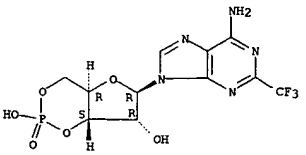
L4 ANSWER 33 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1983:139720 CAPLUS
DOCUMENT NUMBER: 98:139720
TITLE: Evidence that cyclic nucleotides activating rabbit muscle protein kinase I interact with both types of cAMP binding sites associated with the enzyme
AUTHOR(S): Oegreid, Dagfinn; Doeskeland, Stein Ove; Miller, Jon P.
CORPORATE SOURCE: Cell Biol. Res. Group, Preclin. Inst., Bergen, N-5000, Norway
SOURCE: Journal of Biological Chemistry (1983), 258(2), 1041-9
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Eighty different adenine-modified cAMP analogs were tested as activators of rabbit muscle protein kinase I (I) in an in vitro phosphotransferase assay. All of the analogs tested were able to completely activate I. The affinities of the cAMP derivs. for the 2 types (A and B) of binding sites assocd. with the regulatory moiety of I were detd. under conditions similar to those used in the phosphotransferase assay. The potency of the cAMP analogs as I activators correlated with the mean affinity for sites A and B, rather than to the affinity for only 1 of the sites. This was true whether I was assayed at low or near physiol. ionic strength, whether the concn. of I binding site was 0.2 or 400 nM, and whether the I substrate was mixed histones or homogeneous phenylalanine 4-monooxygenase. Furthermore, site A-selective and site B-selective cAMP analogs activated I synergistically. Finally, the degree of synergism between cAMP analogs in activating I correlated with their degree of site selectivity. Thus, cyclic nucleotides interact with both types of binding sites in the process of I activation.
IT **52940-90-6**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(protein kinase activation by, cAMP-binding sites in relation to)
RN 52940-90-6 CAPLUS
CN Adenosine, 2-(trifluoromethyl)-, cyclic 3',5'-(hydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 34 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1982:522897 CAPLUS
DOCUMENT NUMBER: 97:122897
TITLE: Effect of cyclic nucleotide analogs on intrachain site 1 of protein kinase isozymes
AUTHOR(S): Corbin, Jackie D.; Rannels, Stephen R.; Flockhart, David A.; Robinson-Steiner, Alison M.; Tigani, Michael C.; Doeskeland, Stein O.; Suva, Robert H.; Miller, Jon P.
CORPORATE SOURCE: Sch. Med., Vanderbilt Univ., Nashville, TN, 37232, USA
SOURCE: European Journal of Biochemistry (1982), 125(2), 259-66
CODEN: EJBCAI; ISSN: 0014-2956
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of numerous cAMP analogs present in the [3H]cAMP binding reaction on subsequent dissocn. of [3H]cAMP from the regulatory subunit of cAMP-dependent protein kinase I and II were analyzed. Certain analogs with modification at either C-8 or C-2 showed relative selectivity for 1 (site 1) of 2 intrachain cAMP-binding sites of both isoenzymes. Modification at C-6 caused selectivity for the 2nd site (site 2). The combination of a site-1-directed and site-2-directed analog inhibited [3H]cAMP binding much more than did either analog alone. In general, there was a correlation between the site 1 selectivity and the ability of the analog to stimulate the binding of [3H]cIMP, which selects site 2. The site-1-directed analogs stimulated the initial rate of [3H]cIMP binding. The stimulatory effect was enhanced in the presence of a polycationic protein, such as histone, and was inhibited by high ionic strength. The type I and II isoenzymes exhibited large differences in analog specificity for this effect. For type I, of the analogs tested the most efficacious for stimulating [3H]cIMP binding were those contg. a N atom attached to C-8, 8-aminobutylamino-cAMP being the most effective. Type II responded best to analogs contg. a S atom attached to C-8, 8-SH-cAMP being the most effective of those tested. The stimulatory effect was accentuated in the presence of MgATP when using type I, but this nucleotide had no effect when using type II. Thus, in intact tissues cAMP binding to site 1 of either isoenzyme may stimulate the binding to site 2.
IT **52940-90-6**
RL: BIOL (Biological study)
(protein kinase isoenzyme binding of, intrachain site selectivity in relation to)
RN 52940-90-6 CAPLUS
CN Adenosine, 2-(trifluoromethyl)-, cyclic 3',5'-(hydrogen phosphate) (9CI) (CA INDEX NAME)

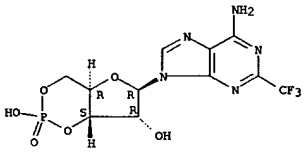
Absolute stereochemistry.



L4 ANSWER 34 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)

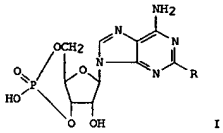
L4 ANSWER 35 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1982:176778 CAPLUS
DOCUMENT NUMBER: 96:176778
TITLE: Cyclic AMP derivatives as tools for mapping cyclic AMP binding sites of cyclic AMP-dependent protein kinases I and II
AUTHOR(S): Miller, Jon P.
CORPORATE SOURCE: Life Sci. Div., SRI Int., Menlo Park, CA, 94025, USA
SOURCE: Advances in Cyclic Nucleotide Research (1981), 14, 335-44
CODEN: ACNRCW; ISSN: 0084-5930
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ability of 48 cAMP analogs with structural modifications in the adenine, ribose, and cyclic phosphate moieties to activate protein kinase (PK) I from rabbit and porcine skeletal muscle and PK II from bovine brain and cardiac muscle was examd. The potency, relative to that of cAMP, of each analog as a PK I or PK II activator is expressed as a Ka' value. Each analog demonstrates comparable Ka' values with the two PK I isozymes, and likewise quite similar Ka' values with the two PK II isozymes. There are a no. of significant differences between the cAMP-binding sites on PK I and those on PK II. The 2 isozymes have clearly different binding locales adjacent to the 2-, 6-, and 8-positions of the adenine ring. PK I and PK II have differential susceptibilities to the effects of alterations in the electron distribution in the adenine ring. The 2 isozymes demonstrate significant differences in the putative binding interactions between the 2'-, 3'-, or 5'-position or the cyclic phosphate moiety and their resp. regulatory subunits. The obsd. differences between the PK I and PK II cAMP binding sites are consistent with the results of spectroscopic studies, which revealed that the cAMP binding sites of the type I and type II regulatory subunits differ considerably, and with the results of partial trypsin hydrolysis, which yielded different cAMP-binding fragments.
IT **52940-90-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(protein kinases I and II activation by, structure in relation to)
RN 52940-90-6 CAPLUS
CN Adenosine, 2-(trifluoromethyl)-, cyclic 3',5'-(hydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 35 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)

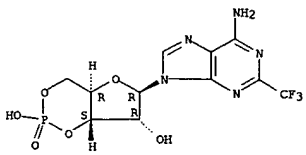
L4 ANSWER 36 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1980:124082 CAPLUS
DOCUMENT NUMBER: 92:124082
TITLE: Mapping cyclic AMP binding sites on type I and type II cyclic AMP-dependent protein kinases using 2-substituted derivatives of cyclic AMP
AUTHOR(S): Yagura, Terry S.; Sigman, Caroline C.; Sturm, Pricilla A.; Reist, Elmer J.; Johnson, Howard L.; Miller, Jon P.
CORPORATE SOURCE: Life Sci. Div., SRI Int., Menlo Park, CA, 94025, USA
SOURCE: Biochemical and Biophysical Research Communications (1980), 92(2), 463-9
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

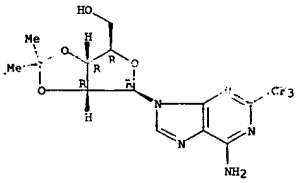
AB Twenty-one derivs. of cAMP (I) (R = alkyl, S-alkyl, Ph, phenethyl, Cl, NH2, etc.) were examd. for their ability to activate rabbit skeletal muscle type I cAMP-dependent protein kinase (PK I) and bovine heart type II cAMP-dependent protein kinase (PK II). PK I had stricter steric requirements than did PK II for the binding locale on the protein kinases adjacent to the 2 position of cAMP. Derivs. with substituents that caused electron withdrawal from the purine ring were better than cAMP as activators of PK I, but were less active than cAMP as activators of PK II.
IT **52940-90-6**
RL: BIOL (Biological study)
(protein kinases activation by, mol. structure in relation to)
RN 52940-90-6 CAPLUS
CN Adenosine, 2-(trifluoromethyl)-, cyclic 3',5'-(hydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



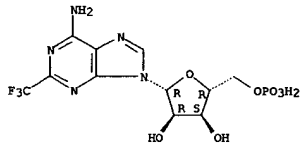
L4 ANSWER 36 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)

L4 ANSWER 37 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)

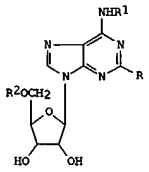


IT **66522-47-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and platelet aggregation inhibition by)
RN 66522-47-2 CAPLUS
CN 5'-Adenylic acid, 2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 37 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1978:416719 CAPLUS
DOCUMENT NUMBER: 89:16719
TITLE: New inhibitors of platelet aggregation. 5'-Phosphate, 5'-phosphorothioate, and 5'-O-sulfamoyl derivatives of 2-substituted adenosine analogs
AUTHOR(S): Gough, Geoffrey R.; Nobbs, Denis M.; Middleton, John C.; Penglis-Caredes, Fylia; Maguire, M. Helen
CORPORATE SOURCE: Dep. Pharmacol., Univ. Sydney, Sydney, Australia
SOURCE: Journal of Medicinal Chemistry (1978), 21(6), 520-5
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



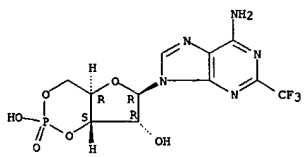
I, $R^2$=P(O)(OH)2
II, $R^2$=$SO_2NH_2$
III, $R^2$=P(S)(OH)2

AB Twelve AMP [61-19-8] analogs I (R = EtS, MeNH, EtNH, EtNH, CF3, Cl, or MeS; R1 = H or Me) and II (R = H, Cl, or MeS; R1 = H) were synthesized from their corresponding nucleosides, via 2',3'-O-isopropylidene derivs., by reaction with 2-cyanoethyl phosphate [2212-88-6] or sulfamoyl chloride [7778-42-9], resp., and subsequent deblocking. In addn., III (R = Cl, MeS, or EtS; R1 = H) were synthesized from the unprotected nucleosides. With the exception of II; (R = H) [25030-31-3] and II; (R = Cl) [66522-52-9], all compds. tested inhibited the ADP-induced aggregation of sheep platelets. The 5'-phosphates and phosphorothioates of 2-methylthio- and 2-ethylthioadenosine were 2-13 times more potent than adenosine. The other I and III were less potent than adenosine. II (R = H) and II (R = Cl) potentiated ADP-mediated platelet aggregation, but II inhibited serotonin-induced platelet aggregation. All I and III analogs tested had negligible activity as inhibitors of serotonin-induced platelet aggregation.
IT **66748-49-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and phosphorylation with cyanoethyl phosphate)
RN 66748-49-0 CAPLUS
CN Adenosine, 2',3'-O-(1-methylethylidene)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 38 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1975:543553 CAPLUS
DOCUMENT NUMBER: 83:143553
TITLE: 2-Substituted derivatives of adenosine and inosine cyclic 3',5'-phosphates. Synthesis, enzymic activity, and analysis of the structural requirements of the binding local [illegible] the 2-substituent on bovine brain protein kinase
AUTHOR(S): Meyer, Rich[illegible], Jr.; [illegible] Hiroshi; Robins, Roland K.; Simon, Lionel N.; [illegible], Jon I.
CORPORATE SOURCE: Nucleic Acid Res. Inst., ICN Pharm., Inc., Irvine, CA, USA
SOURCE: Biochemistry (1975), 14(15), 3315-21
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A number of 2-substituted cyclic nucleotide derivs. were synthesized and investigated as activators of cyclic AMP (I)-dependent protein kinase and as substrates for and inhibitors of I phosphodiesterase. Ring closure of 5-amino-1-.beta.-D-ribofuranosylimidazole-4-carboxamide cyclic 3',5'-phosphate with various aldehydes by a new procedure gave new derivs. of I with the following 2-substituents: Pr, hexyl, octyl, decyl, styryl, o-methoxyphenyl, and 2-thienyl. Alkylation of 2-SH-I gave new I derivs. with the following 2-substituent: EtS, PrS, iso-PrS, allylthio, decylthio, and benzylthio. Deamination of 2-MeS-, 2-BuS-, and 2-EtS-I gave the corresponding 2-substituted cyclic IMP. By the use of multiple regression anal., a striking relationship was found between the relative potency of the compds. as activators of bovine brain I-dependent protein kinase and parameters describing the hydrophobic, steric, and electronic character of the substituents on these compds. All compds. were substrates for a cyclic nucleotide phosphodiesterase prepn. from rabbit kidney. Additionally, the compds. were, as a group, good inhibitors of the hydrolysis of I by phosphodiesterase prepns. from rabbit lung, beef heart, and dog heart.
IT **52940-90-6**
RL: BIOL (Biological study)
(enzyme substrate properties of)
RN 52940-90-6 CAPLUS
CN Adenosine, 2-(trifluoromethyl)-, cyclic 3',5'-(hydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 39 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1974:552585 CAPLUS
DOCUMENT NUMBER: 81:152585
TITLE: Derivatives of cyclic adenosine monophosphate substituted in the 2-position, and their salts
INVENTOR(S): Meyer, Rich Bakke; Shuman, Dennis A.
PATENT ASSIGNEE(S): ICN Pharmaceuticals, Inc.
SOURCE: Ger. Offen., 43 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 2405895 | A1 | 19740829 | DE 1974-2405895 | 19740207 |
| US 3917583 | A | 19751104 | US 1973-330306 | 19730207 |
| BE 810629 | A1 | 19740805 | BE 1974-140566 | 19740205 |
| NL 7401551 | A | 19740809 | NL 1974-1551 | 19740205 |
| FR 2215974 | A1 | 19740830 | FR 1974-3811 | 19740205 |
| JP 49109395 | A2 | 19741017 | JP 1974-14865 | 19740205 |
| CA 1013346 | A1 | 19770705 | CA 1974-191810 | 19740205 |

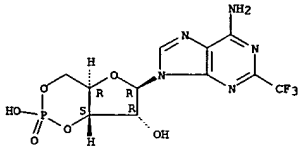
PRIORITY APPLN. INFO.: US 1973-330306 19730207
US 1972-255804 19720522
US 1972-277868 19720804

AB Thirteen tranquilizers I [R = NH2, OH; X = N, N(O); Z = N, CR1, R1 = OH, SH, SMe, alkyl, aryl], with detd. phosphodiesterase inhibiting activity, were prepd. from 5-amino-1-.beta.-D-ribofuranosylimidazole-4-carboxamide, -carboxamidine (II) and -carboxamidooxime 3,5-cyclophosphates. Thus, II 3,5-cyclophosphate treated with MeC(OEt)3 in Me2SO contg. 1,5-diazabicyclo[5.4.0]undec-5-ene at 150.degree. 45 min gave 75% I (R = NH2,X= N, Z = CMe).

IT **52940-90-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 52940-90-6 CAPLUS
CN Adenosine, 2-(trifluoromethyl)-, cyclic 3',5'-(hydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.



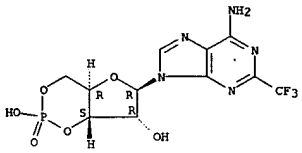
L4 ANSWER 39 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)

L4 ANSWER 40 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1974:491847 CAPLUS
DOCUMENT NUMBER: 81:91847
TITLE: New purine ring closure and the synthesis of 2-substituted derivatives of adenosine cyclic 3',5'-phosphate
AUTHOR(S): Meyer, Rich B., Jr.; Shuman, Dennis A.; Robins, Roland K.
CORPORATE SOURCE: Nucleic Acid Res. Inst., ICN Pharm., Inc., Irvine, CA, USA
SOURCE: Journal of the American Chemical Society (1974), 96(15), 4962-6
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB Cycloadenosines, useful in activating cycloadenosine-dependent protein kinase and inhibiting cAMP phosphodiesterase, were prepd. by treating 5-amino-1-.beta.-D-ribofuranosylimidazole-4-carboxamidine cyclic 3',5'-(hydrogen phosphate) (I) with aldehydes. Thus, I with F3CCONH2 gave II. MeC(OEt)3 and EtC(OEt)3 gave III and IV resp. Eleven other adenosine cyclic phosphates were similarly prepd.

IT **52940-90-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 52940-90-6 CAPLUS
CN Adenosine, 2-(trifluoromethyl)-, cyclic 3',5'-(hydrogen phosphate) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

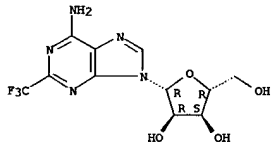


L4 ANSWER 41 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1974:433252 CAPLUS
DOCUMENT NUMBER: 81:33252
TITLE: Coronary dilator actions of adenosine analogs
AUTHOR(S): Cobbin, L. B.; Einstein, Rosemarie; Maguire, M. Helen
CORPORATE SOURCE: Dep. Pharmacol., Univ. Sydney, Sydney, Australia
SOURCE: British Journal of Pharmacology (1974), 50(1), 25-33
CODEN: BJPCBM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Of 23 adenosine (I) [58-61-7] analogs, 22 stimulated coronary blood flow, with potencies which were not related to their durations of action, and durations which were not related to their substrate specificities for adenosine deaminase [9026-93-1] or adenosine kinase [9027-72-9]. Five of the analogs, which were injected intraatrially into anesthetized open thorax dogs, had potencies equal to or greater than that of I, and 4 potentiated the coronary dilator action of I. The duration of this activity may be governed by the rate of tissue uptake of each analog.

IT **4627-40-1 13425-29-1**
RL: BIOL (Biological study)
(coronary dilation from)

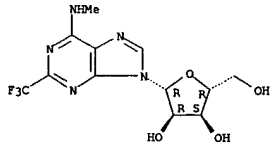
RN 4627-40-1 CAPLUS
CN Adenosine, 2-(trifluoromethyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



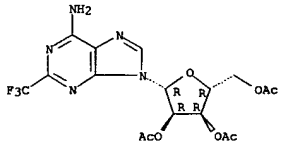
RN 13425-29-1 CAPLUS
CN Adenosine, N-methyl-2-(trifluoromethyl)- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



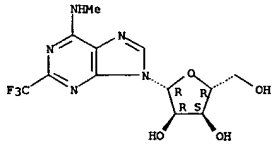
L4 ANSWER 42 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1969:422113 CAPLUS
DOCUMENT NUMBER: 71:22113
TITLE: Preparation of 6-fluoropurines by the modified Schiemann reaction
AUTHOR(S): Montgomery, John A.; Hewson, Kathleen
CORPORATE SOURCE: Kettering- Meyer Lab., Southern Res. Inst., Birmingham, AL, USA
SOURCE: Journal of Organic Chemistry (1969), 34(5), 1396-9
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The use of forcing conditions in the modified Schiemann reaction has now permitted the prepn. of a no. of 6-fluoro- and 2,6-difluoropurines. In the latter cases, the 2-aminoadenines are converted first into the 2-fluoroadenines which nitrosate more favorably than the corresponding adenines and are then converted into the 2,6-difluoropurines.
IT **19768-96-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 19768-96-8 CAPLUS
CN Adenosine, 2-(trifluoromethyl)-, 2',3',5'-triacetate (8CI) (CA INDEX NAME)

Absolute stereochemistry.

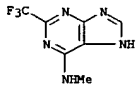


L4 ANSWER 43 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1968:13308 CAPLUS
DOCUMENT NUMBER: 68:13308
TITLE: Biologically active N6-methylated adenosine analogs
AUTHOR(S): Gough, G. R.; Maguire, M. Helen
CORPORATE SOURCE: Univ. Sydney, Sydney, Australia
SOURCE: Journal of Medicinal Chemistry (1967), 10(3), 475-8
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB The synthesis of the vasodilatory title compds. (I) involved the Davoll modification of the classic Fischer-Helferich purine nucleoside synthesis. The appropriate 2-substituted-6-(methylamino)purines were converted to their chloromercuri salts and these were condensed with 2,3,5-tri-O-benzoyl-D-ribosyl chloride. Removal of the Bz blocking groups with MeOH-NH3 gave the required nucleosides. A fusion method was also employed in some cases. 1-O-Acetyl-2,3,5-tri-O-benzoyl-.beta.-D-ribofuranose was fused with a 6-chloropurine in the presence of p-MeC6H4SO3H to give the blocked chloropurine riboside, which was simultaneously deblocked with MeNH2-MeOH at room temp.
IT **13425-29-1P 18925-07-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 13425-29-1 CAPLUS
CN Adenosine, N-methyl-2-(trifluoromethyl)- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

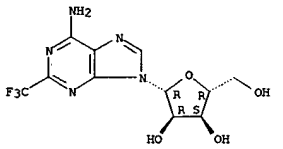


RN 18925-07-0 CAPLUS
CN 1H-Purin-6-amine, N-methyl-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



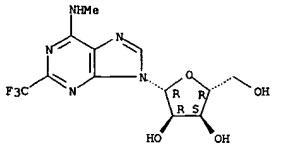
L4 ANSWER 44 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1967:8441 CAPLUS
DOCUMENT NUMBER: 66:8441
TITLE: Adenosine deaminase. I. Purification and properties of ox heart adenosine deaminase
AUTHOR(S): Rockwell, Margaret; Maguire, M. Helen
CORPORATE SOURCE: Univ. Sydney, Sydney, Australia
SOURCE: Molecular Pharmacology (1966), 2(6), 574-84
CODEN: MOPMA3; ISSN: 0026-895X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Adenosine deaminase (I) was purified 1060-fold from ox heart muscle. Adenosine, 2-deoxyadenosine, 2,6-diaminopurine riboside, 6-hydroxylaminopurine riboside, and 6-chloropurine riboside are substrates of the enzyme, and adenosine and deoxyadenosine both exhibit substrate inhibition at concns. .apprx.5-fold greater than the Michaelis value. A no. of 2-substituted adenosine analogs that have vasodilator properties inhibit I competitively, and ouabain is a competitive inhibitor. N6-Methylation of adenosine and of several 2-substituted adenosines gave inhibitors with increased affinity for the active site; however, N6-dimethyladenosine and adenosine-1-N-oxide inhibited noncompetitively. The relation between the structure of the cardioactive adenosine analogs and their affinity for I is considered. 29 references.
IT **4627-40-1 13425-29-1**
RL: BIOL (Biological study)
(adenosine deaminase inhibition by, cardioactivity and)
RN 4627-40-1 CAPLUS
CN Adenosine, 2-(trifluoromethyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 13425-29-1 CAPLUS
CN Adenosine, N-methyl-2-(trifluoromethyl)- (8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.



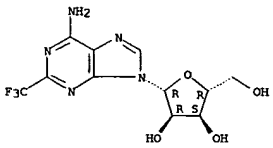
L4 ANSWER 44 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)

L4 ANSWER 45 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1966:4358 CAPLUS
DOCUMENT NUMBER: 64:4358
ORIGINAL REFERENCE NO.: 64:792g-h,793a
TITLE: 2-Trifluoromethyladenosine
AUTHOR(S): Gough, G.; Maguire, M. H.
CORPORATE SOURCE: Univ. Sydney
SOURCE: Journal of Medicinal Chemistry (1965), 8(6), 866-7
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 2-Trifluoromethyladenosine (I) was synthesized to evaluate its vasodilator and antiagglutination effects. A mixt. of 5.86 g. 2-trifluoromethyl-6-chloropurine and 12.8 g. 1-O-acetyl-2,3,5-tri-O-benzoyl-.beta.-D-ribofuranose was heated in vacuo at 130-5.degree. until a clear orange melt was obtained. The mixt. was cooled, 20 mg. p-toluenesulfonic acid added and the mixt. reheated in vacuo at 135.degree. for 35 min. when vigorous evolution of gas took place. The cooled residue was dissolved in 100 ml. CHCl3 and the soln. washed with aq. NaHCO3 and H2O, and dried to give 16.2 g. powder, [.alpha.]D - 54.9 .+-. 0.9.degree. (c 1.02, CHCl3). It was dissolved in MeOH and satd. with NH3 at 0.degree. and soln. kept at room temp. for 5 days. Evapn. and trituration of the residue with CHCl3 gave 7.1 g. powder which on crystn. from 1-propanol and H2O gave 2.5 g. I, m. 194-5.degree., [.alpha.]D -51.8 .+-. 0.4.degree. (c 0.922, MeOH), .lambda.pHilmax. 256 m.mu. (.epsilon. 10,400), .lambda.pH 13max. 255 m.mu. (.epsilon. 12,600). I was much less active than 2-chloroadenosine in the inhibition of the adenosine diphosphate induced agglutination of platelets and it showed only weak vasodilator activity in the isolated cat hind limb.

IT **4627-40-1**, Adenosine, 2-(trifluoromethyl)-
(prepn. of)
RN 4627-40-1 CAPLUS
CN Adenosine, 2-(trifluoromethyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)

Absolute stereochemistry.

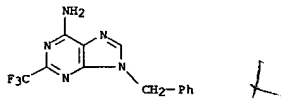


L4 ANSWER 46 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1964:68223 CAPLUS
DOCUMENT NUMBER: 60:68223
ORIGINAL REFERENCE NO.: 60:12013a-b
TITLE: Fluorine-containing potential anticancer agents. II. Syntheses of some trifluoromethylpurines and trifluoromethylthiazolopyrimidines
AUTHOR(S): Nagano, Hideo; Inoue, Shoji; Saggiomo, Andrew J.; Nodiff, Edward A.
CORPORATE SOURCE: Temple Univ., Philadelphia, PA
SOURCE: Journal of Medicinal Chemistry (1964), 7(2), 215-20
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

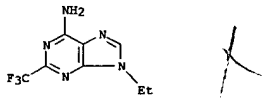
GI For diagram(s), see printed CA Issue.

AB cf. CA 57, 824f. Various trifluoromethylpyrimidines were prepd. and cyclized by standard techniques to the corresponding trifluoromethylpurines (I) and thiazolo[5,4-d]pyrimidines (II). Compds. prepd. were evaluated as tumor inhibitors; all were ineffective.

IT **1643-90-9**, Adenine, 9-benzyl-2-(trifluoromethyl)-
**1736-95-4**, Adenine, 9-ethyl-2-(trifluoromethyl)- **1814-73-9**, Adenine, N,9-diphenyl-2-(trifluoromethyl)- **2248-26-2**, Adenine, N,9-diethyl-2-(trifluoromethyl)- **2262-34-2**, Adenine, N,9-dibutyl-2-(trifluoromethyl)- **2789-03-9**, Adenine, 9-methyl-2-(trifluoromethyl)-
(prepn. of)
RN 1643-90-9 CAPLUS
CN 9H-Purin-6-amine, 9-(phenylmethyl)-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

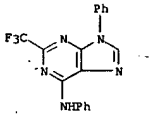


RN 1736-95-4 CAPLUS
CN Adenine, 9-ethyl-2-(trifluoromethyl)- (7CI, 8CI) (CA INDEX NAME)

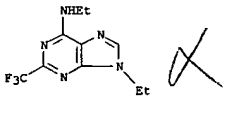


RN 1814-73-9 CAPLUS
CN Adenine, N,9-diphenyl-2-(trifluoromethyl)- (7CI, 8CI) (CA INDEX NAME)

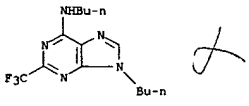
L4 ANSWER 46 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)



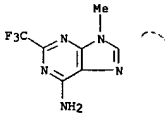
RN 2248-26-2 CAPLUS
CN Adenine, N,9-diethyl-2-(trifluoromethyl)- (7CI, 8CI) (CA INDEX NAME)



RN 2262-34-2 CAPLUS
CN Adenine, N,9-dibutyl-2-(trifluoromethyl)- (7CI, 8CI) (CA INDEX NAME)



RN 2789-03-9 CAPLUS
CN Adenine, 9-methyl-2-(trifluoromethyl)- (7CI, 8CI) (CA INDEX NAME)



L4 ANSWER 47 OF 47 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1959:51177 CAPLUS
DOCUMENT NUMBER: 53:51177
ORIGINAL REFERENCE NO.: 53:9234h-i,9235a-i,9236a-g
TITLE: Fluorine-containing pyrimidines and purines: synthesis and properties of trifluoromethyl pyrimidines and purines
AUTHOR(S): Giner-Sorolla, Alfredo; Bendich, Adrien
CORPORATE SOURCE: Cornell Univ. Med. Coll., New York, NY
SOURCE: Journal of the American Chemical Society (1958), 80, 5744-52
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB PhNH2 (52 g.) in 160 cc. concd. HCl diazotized at 0.degree. with 43.5 g. NaNO2 in 90 cc. H2O, treated slowly with stirring with 450 g. NaOAc in 1 l. H2O at 0.degree., treated dropwise with stirring at 0.degree. with 112 g. CF3COCH2CO2Et (I) in 90 cc. EtOH, stirred 4 hrs. at 0.degree., kept overnight at room temp. and filtered yielded 136 g. CF3COCH(CO2Et)N:NPh (II), m. 77-8.degree.. A sample of II hydrogenated in EtOH at room temp. and atm. pressure over Raney Ni gave CF3COCH(NH2)CO2Et, m. 200-2.degree.. CS(NH2)2 (1.52 g.) added to 0.46 g. Na in 30 cc. BuOH, the refluxing mixt. treated with stirring with 5.76 g. II, refluxed 3 hrs. with stirring, please stored overnight, concd. in vacuo, dild. with 200 cc. H2O, and filtered, the filtrate acidified to pH 5 with 20% AcOH, and the red ppt. filtered off and washed with cold H2O gave 5.5 g. 4-hydroxy-2-mercapto-5-phenylazo-6-trifluoromethylpyrimidine (III), orange needles, m. 168-72.degree. (decompn.) (EtOH). III (3.5 g.) in 100 cc. H2O contg. 3.5 cc. concd. NH4OH refluxed 1 hr. with stirring with 18 g. Raney Ni, and filtered hot, the residue boiled with 30 cc. H2O and filtered, the combined filtrates further refluxed 45 min. with 10 g. fresh Raney Ni and 1 cc. concd. NH4OH, the mixt. filtered, the residue boiled with 80 cc. H2O and filtered, and the combined filtrates evapd. in vacuo on the steam bath yielded 1.1 g. 5-amino-4-hydroxy-6-trifluoromethylpyrimidine (IV), yellow needles, m. 222.degree. (H2O). IV (7.0 g.), 16 cc. 98% HCO2H, and 32 cc. Ac2O heated 5 min. at 40.degree. and 30 min. at 70.degree. and concd. in vacuo yielded 8.6 g. (crude) 5-OHCNH analog (V) of IV, needles, m. 195-6.degree. (EtOH). The crude V refluxed 1 hr. with stirring with 30 cc. POCl3, concd. to about 1/3 of the original vol., cooled, poured onto 150 g. crushed ice, stirred 15 min., and filtered, the residue added to 200 cc. cold satd. alc. NH3, refrigerated overnight, and evapd. in vacuo, the black tarry residue (3.7 g.) boiled 15 min. with 15 cc. HCONH2, cooled, dild. with 5 cc. H2O, chilled overnight, filtered, and evapd. in vacuo, and the brown residue washed with a little H2O and dried gave 0.6 g. 6-trifluoromethylpurine (VI), needles, m. 254-5.degree. (decompn.). 4-Hydroxy-2-mercapto-6-trifluoromethylpyrimidine (VII) (10 g.) slowly added to 40 cc. POCl3 at 20-5.degree., treated dropwise at 20-5.degree. with 13 cc. PhNEt2, treated again with 20 cc. POCl3, refluxed 2 hrs. with stirring, about 1/2 of the POCl3 distd. in vacuo, the crude mixt. cooled, poured onto 500 g. crushed ice, stirred 15 min., and filtered, the residue washed with cold H2O, poured into 150 cc. EtOH satd. with NH3, chilled overnight, and filtered, the filtrate evapd. in vacuo, the residue extd. with Et2O, and the ext. poured into petr. ether yielded 3.0 g. 4-NH2 analog (VIII) of VII, needles, m. 203-5.degree. (H2O). VII (3.4 g.) in 2 cc. concd. NH4OH in 50 cc. H2O refluxed 1.5 hrs. with stirring, filtered hot, the residue extd. with 15 cc. boiling H2O, and the combined filtrates evapd. yielded 2.5 g. 4-hydroxy-6-trifluoromethylpyrimidine (IX), needles, m. 162-3.degree. (sublimed at 120.degree./0.1 mm.). IX (4 g.) treated with POCl3 and PhNEt2 by the method described for the prepn. of VIII yielded 2.3 g. 4-NH2 analog (X) of IX, yellow prisms, m. 165-70.degree..

L4 ANSWER 47 OF 47 CAPLUS COPYRIGHT 2003 ACS (Continued)
VIII (1 g.) and 10 g. Raney Ni in 50 cc. M NH4OH refluxed 4 hrs. with stirring gave 0.3 g. X, prisms, m. 168-70.degree.. VII (1.96 g.) refluxed 4 hrs. with 0.95 g. ClCH2CO2H in 20 cc. H2O and cooled gave 1.55 g. 2-HO2CCH2S analog (XI) of VII, m. 205-7.degree. (H2O). XI (1.0 g.) in 15 cc. 6N HCl refluxed 5 hrs. and chilled yielded 0.68 g. 2,4-dihydroxy-6-trifluoromethylpyrimidine (XII), plates or prisms, m. 218-20.degree.. Urea (3.0 g.) and 1.15 g. Na refluxed with stirring in 20 cc. BuOH, the soln. treated with 9.6 g. I, refluxed 3 hrs. with stirring, cooled, filtered, adjusted with concd. HCl to pH 5, and filtered gave 0.3 g. XII, prisms, m. 220-2.degree.. Na (4.60 g.) in 80 cc. BuOH refluxed 15 min. with stirring with 9.55 g. dry H2NC(:NH)NH2.HCl, treated with 18.4 g. I, refluxed 4 hrs., chilled, decolorized with C, adjusted with glacial AcOH to pH 5, and filtered yielded 13.0 g. 2-NH2 deriv. (XIII) of IX, needles, m. 282.degree.. XIII (2.7 g.) in 25 cc. CCl4 treated dropwise with 1.6 g. Br, refluxed 26 hrs., and evapd., and the residue (6.2 g.) dissolved in 50 cc. 2N NaOH, decolorized with C, adjusted with glacial AcOH to pH 5, and repptd. twice in the same manner yielded 3.0 g. 5-Br deriv. (XIV) of XIII, needles, m. 303.degree. (decompn.). XIII (3.98 g.) heated on the steam bath with 3.3 g. Br in 20 cc. glacial AcOH and evapd. in vacuo yielded 3.6 g. XIV, m. 298.degree. (decompn.) (H2O). XIV was not changed by refluxing 0.5 hr. with 10N KOH. XIV heated 2 hrs. in a sealed tube with concd. NH4OH at 160.degree. gave only F-free material. Dry H2NC(:NH)NH2.HCl (6.8 g.) refluxed 15 min. with 3.6 g. Na in 80 cc. BuOH, treated with 20.6 g. II, refluxed 3 hrs. with stirring, and filtered, and the residue dissolved in 300 cc. boiling H2O, treated with C, and repptd. with glacial AcOH (pH 5) yielded 16.4 g. 5-PhN:N deriv. (XV) of XIII, m. 280-2.degree.. XV (6.7 g.) treated in the usual manner with POCl3 and PhNEt2 yielded 3.0 g. 4-NH2 analog (XVI) of XV, yellow prisms, m. 235-6.degree. (sublimed at 160.degree./0.1 mm.). XVI (5.0 g.) in 200 cc. abs. EtOH hydrogenated under ambient conditions over 5.0 g. 5% Pd-C, filtered, and evapd. in vacuo, the residue treated with 10 cc. 98% HCO2H, and the mixt. evapd. gave 3.5 g. (crude) 2,4,5-triamino-6-trifluoromethylpyrimidine (XVII), prisms, m. 196-8.degree. (EtOH). Crude XVII (1.5 g.) in 10 cc. 98% HCO2H refluxed 0.5 hr. at 110.degree. under CO2 and evapd., the residue heated 45 min. at 210-15.degree., the brown residue refluxed 3 hrs. with 50 cc. EtOH and 0.3 g. CaCO3, treated with C, and filtered, the residue extd. 0.5 hr. with 30 cc. boiling EtOH, and the combined filtrates concd. in vacuo to about 15 cc. and cooled yielded 0.35 g. 2-NH2 deriv. (XVIII) of VI, needles, m. 360.degree. (decompn.) (EtOH). XVII (2 g.) in 10 cc. CF3CO2H and 2 cc. (CF3CO)2O (XIX) refluxed 1 hr. under CO2 and evapd., the residue kept 1 hr. at 210-15.degree., and the dark residue refluxed 3 hrs. with 30 cc. H2O and 0.5 g. CaCO3, treated with C, and cooled gave 0.8 g. 2-amino-6,8-bis(trifluoromethyl)purine (XX), needles, m. 230.degree. (H2O), also obtained in lower yield from XVII and CF3CONH2 at 180.degree. during 1 hr. 4,5-Diaminopyrimidine (2 g.) in 10 cc. XIX refluxed 2 hrs. under CO2, the XIX distd., the residue heated 45 min. at 210.degree. under CO2, heated in vacuo at 210.degree., the residue (2.8 g.) extd. with 40 cc. boiling EtOH and 0.5 g. CaCO3, treated with C, and filtered through diatomaceous earth, the extn. with EtOH repeated, and the combined filtrates concd. to 15 cc. and refrigerated 5 hrs. gave 1.2 g. 8-trifluoromethylpurine (XXI), needles, m. 192.degree. (sublimed at 90.degree./0.1 mm.). 2,4,5,6-Tetraaminopyrimidine (2.5 g.) in 20.5 g. CF3CO2H refluxed 1 hr. under CO2, the CF3CO2H distd., the residue heated 1 hr. under CO2 at 210.degree., and recrystd. from 3:2 AcOH-EtOH, and the crude product (1.85 g.) sublimed at

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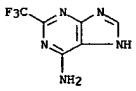
250.degree./0.1 mm. and recrystd. from H2O gave 2,6-diamino deriv. (XXII) of XXI.2H2O in 2 crystal forms, both m. above 300.degree.. 6-Chloro-4,5-diaminopyrimidine (2 g.) in 20 cc. CF3CO2H and 10 cc. XIX refluxed 3 hrs. and evapd. in vacuo, the residue heated 1 hr. to 260.degree. under CO2 and then in vacuo, the brown solid residue (2.8 g.) extd. with 100 cc. EtOH contg. 0.4 g. CaCO3, the filtrate concd. in vacuo to about 20 cc., and cooled gave 2.2 g. 6-OH deriv. (XXIII) of XXI, m. 322-4.degree. (decompn.) (H2O). 4,5,6-Triaminopyrimidine (1.5 g.) and 8.1 g. CF3CONH2 refluxed 2 hrs. and the product washed with Et2O and H2O yielded 1.95 g. 6-NH2 deriv. of XXI, m. 330-5.degree. (50% aq. EtOH). 4-Amino-5-imidazolecarboxamide-HCl (1 g.) and 6.8 g. CF3CONH2 refluxed 4 hrs. gave similarly 1 g. 2-trifluoromethyl-6-hydroxypurine (XXIV), needles, m. 324-6.degree. (decompn.) (MeOH). 4-Amino-5-imidazolecarboxamidine-2HCl (2.4 g.) and 13.5 g. CF3CONH2 refluxed 2 hrs., cooled, washed with Et2O, and recrystd. from 50% EtOH yielded 1.4 g. 6-NH2 analog of XXIV, needles (50% aq. EtOH). The apparent pKa values were detd. spectroscopically for the following compds. (soly. at 20.degree. in H2O in parts of H2O/part material, and pKa values in H2O given): 6-methylpurine (m. 235-6.degree.), 5, 9.02, 2.6; VI, -, 7.35, less than 0; 8-methylpurine (m. 271-3.degree.), 18, 9.37, 2.85; XXI, 15, 5.12, 1.0; 2-aminopurine, 120, 9.93, 3.80, -0.28; XVIII, 6700, 8.87, 1.85; XX, 705, 5.02, about 0.3; 2,6-diaminopurine, 420, 10.77, 5.09, less than 1; XXII, 2400, 7.55, 3.68; 6-hydroxypurine, 1400, 12.10, 8.94, 1.98; XXIV, 890, 11.2, 5.1, about 1.1; XXIII, 610, 10.9, about 5; uracil (m. 338.degree.), 280, above 13, 9.5; XII, 340, about 13, 5.7. The ultraviolet absorption max. of all these compds. are listed. The ultraviolet absorption spectrum of XII is recorded.

IT **2993-06-8**, Adenine, 2-(trifluoromethyl)-
(prepn. of)

RN 2993-06-8 CAPLUS

CN 1H-Purin-6-amine, 2-(trifluoromethyl)- (9CI) (CA INDEX NAME)



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| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| FULL ESTIMATED COST | 214.03 | 362.39 |

| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
|---|---|---|
| CA SUBSCRIBER PRICE | -30.60 | -30.60 |

STN INTERNATIONAL LOGOFF AT 10:29:16 ON 04 JUN 2003

Species

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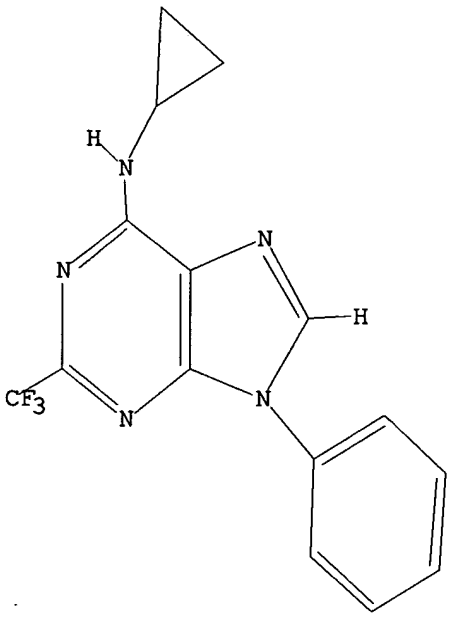


Structure attributes must be viewed using STN Express query preparation.

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SEARCH TIME: 00.00.01

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BATCH **COMPLETE**
PROJECTED ITERATIONS: 9 TO 360
PROJECTED ANSWERS: 1 TO 80

L2 1 SEA SSS SAM L1

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FULL SCREEN SEARCH COMPLETED - 138 TO ITERATE

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SEARCH TIME: 00.00.01

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